Atty. Dkt. No.: 039363-1202

U.S. PATENT APPLICATION

for

PYK2 CRYSTAL STRUCTURE AND USES

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CROSS-REFERENCE TO RELATED PATENT APPLICATIONS

[0001] This application claims the benefit of Ibrahim et al., U.S. Provisional Application 60/451,101, filed February 28, 2003, which is incorporated herein by reference in its entirety, including drawings.

BACKGROUND OF THE INVENTION

[0002] This invention relates to the field of development of ligands for protein tyrosine kinase 2 (PYK2) and to the use of crystal structures of PYK2. The information provided is intended solely to assist the understanding of the reader. None of the information provided nor references cited is admitted to be prior art to the present invention.

[0003] Cellular signal transduction is a fundamental mechanism whereby external stimuli that regulate diverse cellular processes are relayed to the interior of cells. One of the key biochemical mechanisms of signal transduction involves the reversible phosphorylation of tyrosine residues on proteins. The phosphorylation state of a protein is modified through the reciprocal actions of tyrosine phosphatases (TPs) and tyrosine kinases (TKs), including receptor tyrosine kinases and non-receptor tyrosine kinases.

[0004] Receptor tyrosine kinases (RTKs) belong to a family of transmembrane proteins and have been implicated in cellular signaling pathways. The predominant biological activity of some RTKs is the stimulation of cell growth and proliferation, while other RTKs are involved in arresting growth and promoting differentiation. In some instances, a single tyrosine kinase can inhibit, or stimulate, cell proliferation depending on the cellular environment in which it is expressed.

[0005] RTKs are composed of at least three domains: an extra-cellular ligand binding domain, a transmembrane domain and a cytoplasmic catalytic domain that can phosphorylate tyrosine residues. Ligand binding to membrane-bound receptors induces

the formation of receptor dimers and allosteric changes that activate the intracellular kinase domains and result in the self-phosphorylation (autophosphorylation and/or transphosphorylation) of the receptor on tyrosine residues. Individual phosphotyrosine residues of the cytoplasmic domains of receptors may serve as specific binding sites that interact with a host of cyto-plasmic signaling molecules, thereby activating various signal transduction pathways.

[0006] The intracellular, cytoplasmic, non-receptor protein tyrosine kinases do not contain a hydrophobic transmembrane domain or an extracellular domain and share non-catalytic domains in addition to sharing their catalytic kinase domains. Such non-catalytic domains include the SH2 domains and SH3 domains. The non-catalytic domains are thought to be important in the regulation of protein-protein interactions during signal transduction.

[0007] A central feature of signal transduction is the reversible phosphorylation of certain proteins. Receptor phosphorylation stimulates a physical association of the activated receptor with target molecules, which either are or are not phosphorylated.

[0008] Some of the target molecules such as phospholipase Cγ are in turn phosphorylated and activated. Such phosphorylation transmits a signal to the cytoplasm. Other target molecules are not phosphorylated, but assist in signal transmission by acting as adapter molecules for secondary signal transducer proteins. For example, receptor phosphorylation and the subsequent allosteric changes in the receptor recruit the Grb-2/SOS complex to the catalytic domain of the receptor where its proximity to the membrane allows it to activate ras.

[0009] The secondary signal transducer molecules generated by activated receptors result in a signal cascade that regulates cell functions such as cell division or differentiation. Reviews describing intracellular signal transduction include Aaronson, *Science* 254:1146-1153, 1991; Schlessinger, *Trends Biochem. Sci.*, 13:443-47, 1988; and Ullrich and Schlessinger, *Cell*, 61:203-212, 1990.

[0010] Signal transduction pathways that regulate ion channels (e.g., potassium channels and calcium channels) involve G proteins which function as intermediaries between receptors and effectors. Gilman, *Ann. Rev. Biochem.*, 56:615-649 (1987); Brown and

Birnbaumer, *Ann. Rev. Physiol.*, 52: 197-213 (1990). G-coupled protein receptors are receptors for neurotransmitters, ligands that are responsible for signal production in nerve cells as well as for regulation of proliferation and differentiation of nerves and other cell types. Neurotransmitter receptors exist as different subtypes which are differentially expressed in various tissues and neurotransmitters such as acetylcholine evoke responses throughout the central and peripheral nervous systems.

[0011] The muscarinic acetylcholine receptors play important roles in a variety of complex neural activities such as learning, memory, arousal and motor and sensory modulation. These receptors have also been implicated in several central nervous system disorders such as Alzheimer's disease, Parkinson's disease, depression and schizophrenia.

[0012] Some agents that are involved in a signal transduction pathway regulating one ion channel, for example a potassium channel, may also be involved in one or more other pathways regulating one or more other ion channels, for example a calcium channel. Dolphin, *Ann. Rev. Physiol.*, 52:243-55 (1990); Wilk-Blaszczak et al., *Neuron*, 12: 109-116 (1994). Ion channels may be regulated either with or without a cytosolic second messenger. Hille, *Neuron*, 9:187-195 (1992). One possible cytosolic second messenger is a tyrosine kinase. Huang et al., *Cell*, 75:1145-1156 (1993), incorporated herein by reference in its entirety, including any drawings.

[0013] The receptors involved in the signal transduction pathways that regulate ion channels are ultimately linked to the ion channels by various intermediate events and agents. For example, such events include an increase in intracellular calcium and inositol triphosphate and production of endothelin. Frucht, et al., *Cancer Research*, 52:1114-1122 (1992); Schrey, et al., *Cancer Research*, 52:1786-1790 (1992). Intermediary agents include bombesin, which stimulates DNA synthesis and the phosphorylation of a specific protein kinase C substrate. Rodriguez-Pena, et al., *Biochemical and Biophysical Research Communication*, 140(1):379-385 (1986); Fisher and Schonbrunn, *J. Biol. Chem.*, 263(6):2208-2816 (1988).

[0014] Focal adhesion kinase (FAK) is a cytoplasmic protein tyrosine kinase localized to focal adhesions that is known to associate with two Src family kinases. Schaller, et al., *Proc. Natl. Acad. Sci. U.S.A.*, 89:5192-5196 (1992), incorporated herein by reference in its entirety, including any drawings; Cobb et al., *Mol. Cell. Biol.*, 14(1):147-155 (1994). The

proteins associated with the cytoplasmic surface of adhesion molecules are reviewed in Gumbiner, *Neuron*, 11:551-564 (1993).

[0015] FAK may regulate interactions of integrins, agonist receptors, and/or stress fibers. Shattil et al., *J. Biol. Chem.*, 269(20):14738-14745 (1994); Ridley and Hall, *The EMBO Journal*, 13(11):2600-2610 (1994). FAK does not contain SH2 or SH3 domains and the amino acid sequence of FAK is highly conserved among birds, rodents and man.

[0016] In some cells the C-terminal domain of FAK is expressed autonomously as a 41 kDa protein called FRNK and the 140 C-terminal residues of FAK contain a focal adhesion targeting (FAT) domain. The cDNA's encoding FRNK are given in Schaller et al., *Mol. Cell. Biol.*, 13(2) :785-791 (1993), incorporated herein by reference in its entirety, including any drawings. The FAT domain was identified and said to be required for localization of FAK to cellular focal adhesions in Hilderbrand et al., *J. Cell Biol.*, 123(4):993-1005 (1993).

[0017] The non-receptor tyrosine kinase, PYK2, is activated by binding of ligand to G-coupled protein receptors such as bradykinin and acetylcholine. PYK2 has a predicted molecular weight of 111 kD and contains five domains: (1) a relatively long N-terminal domain; (2) a kinase catalytic domain; (3) a proline rich domain; (4) another proline rich domain; and (5) a C-terminal focal adhesion targeting (FAT) domain. PYK2 does not contain a SH2 or SH3 domain.

[0018] The FAT domain of PYK2 has 62% similarity to the FAT domain of another non-receptor tyrosine kinase, FAK, which is also activated by G-coupled proteins. The overall similarity between PYK2 and FAK is 52%. PYK2 is expressed principally in neural tissues, although expression can also be detected in hematopoietic cells at early stages of develop-ment and in some tumor cell lines. The expression of PYK2 does not correspond with the expression of FAK.

[0019] PYK2 is also known as Cell Adhesion Kinase β (CAK β) and Related Adhesion Focal Tyrosine Kinase (RAFTK). Nucleotide and amino acid sequences for PYK2 are described in a set of related patents, including U.S. Patent 8,837,815; 5,837,524; and Patent Publication U.S. 2002/0048782, which also provided additional information on PYK2 and a related protein, FAK, including some of the information described below.

Each of these documents describes nucleotide and amino acid sequences for PYK2. Patent 5,837,524 describes a method of screening for agents "able to promote or disrupt the interaction" between "a PYK2 polypeptide and a natural binding partner (NBP)." (Col. 8, lines 60-67.) Patent Publication U.S. 2002/0048782 provides examples describing cloning and the testing of certain properties of PYK2. Each of these patents and patent publication are incorporated by reference herein in their entireties, including drawings.

[0020] PYK2 is believed to regulate the activity of potassium channels in response to neurotransmitter signalling. PYK2 enzymatic activity is positively regulated by phosphorylation on tyrosine and results in response to binding of bradykinin, TPA, calcium ionophore, carbachol, TPA+ forskolin, and membrane depolarization. The combination of toxins known to positively regulate G-coupled receptor signalling (such as pertusis toxin, cholera toxins, TPA and bradykinin) increases the phosphorylation of PYK2. Activated PYK2 phosphorylates RAK, a delayed rectifier type potassium channel, and thus suppresses RAK activity. In the same system, FAK does not phosphorylate RAK.

[0021] Further, integrin-linked signaling is important for regulating cell adhesion and motility. (Hynes, R. (2002) Integrins: bidirectional, allosteric signaling machines. *Cell*, **110**, 673-687.) The FAK and PYK2 tyrosine kinases are key mediators of integrin-dependent signals. (Hauck *et al.* (2000) Focal adhesion kinase functions as a receptor-proximal signaling component required for directed cell migration. *Immunol Res*, **21**, 293-303.) Both FAK and PYK2 mediate cytoskeletal rearrangements as a consequence of integrin ligation. FAK, which localizes to focal adhesions, is activated by binding of cell-surface integrins to the extracellular matrix. In response to external stimuli, growth factors associate with integrins, and FAK also becomes phosphorylated in response to growth factors. (Sieg, et al. (2000) FAK integrates growth-factor and integrin signals to promote cell migration. *Nat Cell Biol*, **2**, 249-256.) In addition to its role in regulating the cytoskeleton and cell movements, FAK also helps to coordinate these processes with growth signals and cellular survival.

[0022] By contrast, PYK2 is localized to the sites of cell-cell contacts, and becomes activated in response to calcium mobilization. (Lev, et al. (1995) Protein tyrosine kinase PYK2 involved in Ca(2+)-induced regulation of ion channel and MAP kinase functions.

Nature, **376**, 737-745.) Indeed, whereas FAK appears to mediate cellular survival, PYK2 activation leads to apoptosis in fibroblasts. (Xiong, W. and Parsons, J.T. (1997) Induction of apoptosis after expression of PYK2, a tyrosine kinase structurally related to focal adhesion kinase. *J Cell Biol*, **139**, 529-539.) In monocytes and osteoclasts, PYK2 localizes to the podosome, a cellular protrusion that contacts the extracellular matrix and mediates adhesion and motility in these cell types. (Duong *et al.* (1998) PYK2 in osteoclasts is an adhesion kinase, localized in the sealing zone, activated by ligation of alpha(v)beta3 integrin, and phosphorylated by src kinase. *J Clin Invest*, **102**, 881-892; Lakkakorpi et al. (1999) Stable association of PYK2 and p130(Cas) in osteoclasts and their co-localization in the sealing zone. *J Biol Chem*, **274**, 4900-4907.)

[0023] In spite of the different biological functions, FAK and PYK2 are the only members of the FAK family of tyrosine kinases, and they share 45% sequence identity overall, with higher homology in the kinase catalytic domain (60%). (Lev et al. (1995) *Nature*, **376**, 737-745; Sasaki et al. (1995) Cloning and characterization of cell adhesion kinase beta, a novel protein-tyrosine kinase of the focal adhesion kinase subfamily. *J Biol Chem*, **270**, 21206-21219.) Furthermore, most of the key regulatory sites are highly conserved. In the N-terminus is a large integrin-binding domain. In the C-terminus is the so-called FAT (focal adhesion targeting) domain that mediates subcellular localization via binding sites for the cytoskeleton-associated proteins paxillin and talin. The kinase catalytic domain is in the center of the proteins. In addition, proline-rich regions in the C-terminus serve to bind to the SH3 domains of the adaptor proteins CAS and GRAF. (Hildebrand et al. (1996) An SH3 domain-containing GTPase-activating protein for Rho and Cdc42 associates with focal adhesion kinase. *Mol Cell Biol*, **16**, 3169-3178; Polte, T.R. and Hanks, S.K. (1995) Interaction between focal adhesion kinase and Crk-associated tyrosine kinase substrate p130Cas. *Proc Natl Acad Sci U S A*, **92**, 10678-10682.)

[0024] The primary autophosphorylation site (Y397 in FAK, Y402 in PYK2, just upstream of the catalytic domain) serves as a binding site for the SH2 domain of a Src-family tyrosine kinase. (Dikic et al. (1996) A role for Pyk2 and Src in linking G-protein-coupled receptors with MAP kinase activation. *Nature*, **383**, 547-550.) This site is also a substrate for the Src kinase. Additional tyrosine phosphorylation events occur at residues within the catalytic domain (Y576, Y577 in FAK, Y579, Y580 in PYK2) whose function is unclear, and at a C-terminal site (Y925 in FAK, Y881 in PYK2) that serves as binding

site for the SH2 domain of GRB2. (Schlaepfer et al. (1999) Signaling through focal adhesion kinase. *Prog Biophys Mol Biol*, **71**, 435-478.) In addition to assembling a variety of proteins, FAK and PYK2 also play important roles by phosphorylating key substrates such as paxillin and CAS. (Bellis et al. (1995) Characterization of tyrosine phosphorylation of paxillin in vitro by focal adhesion kinase. *J Biol Chem*, **270**, 17437-17441; Li, X. and Earp, H.S. (1997) Paxillin is tyrosine-phosphorylated by and preferentially associates with the calcium-dependent tyrosine kinase in rat liver epithelial cells. *J Biol Chem*, **272**, 14341-14348.) Tyrosine phosphorylation of paxillin and CAS creates a new binding site for SH2 adaptor proteins. For example, paxillin binds to and is phosphorylated by PYK2 in hematopoietic cells. (McShan *et al.* (2002) Csk homologous kinase associates with RAFTK/Pyk2 in breast cancer cells and negatively regulates its activation and breast cancer cell migration. *Internat. J. Oncology* **21**:197-205.)

[0025] Furthermore, expression of PYK2 and FAK was observed in breast cancer cells, and it was reported that PYK2 participates in intracellular signaling upon heregulin (HRG) stimulation and promotes breast carcinoma invasion. CHK acted as a negative regulator of PYK2, significantly reducing the migration of PYK2 expressing breast cancer cells. (McShan *et al.* (2002) *Internat. J. Oncology* **21**:197-205.)

[0026] Methods of identifying a compound that binds to and/or modulates the activity of PYK2 are described in Duong et al., PCT/US98/02797, WO 98/35056, where the method involves contacting the compound and PYK2 and determining if binding has occurred. If binding has occurred, the activity of the bound PYK2 can be compared to the activity of PYK2 which is not bound to the compound to determine if the compound modulates PYK2 activity. (p.2, lines 9-15) The compounds identified are indicated to be useful in the prevention or teatment of osteoporosis, inflammation, and other conditions dependent on monocyte migration and invasion activities. (p.3, lines 1-5) This application is hereby incorporated by reference in its entirety.

SUMMARY OF THE INVENTION

[0027] The present invention concerns structural information about PYK2 kinase, crystals of PYK2 kinases with and without binding compounds, and the use of the PYK2

kinase crystals and structural information about the PYK2 kinase to develop PYK2 ligands, *e.g.*, inhibitors.

[0028] Thus, in a first aspect, the invention concerns a method for determining the orientation of compounds that bind to PYK2 and/or identifying binding compounds by determining the orientation of at least one compound bound to PYK2 in co-crystals of PYK2 with binding compound. The method also characterizes the binding of a PYK2 binding compound bound to PYK2. In particular embodiments, the method can also involve one or more of: identifying as molecular scaffolds one or more compounds that bind weakly (with low or very low affinity) to a binding site of PYK2 kinase and have molecular weight less than 350 daltons; determining activity of the compounds or molecular scaffolds against PYK2 (activity can also be determined against 1, 2, 3, or more additional kinases; scaffolds preferably have low activity); determining the orientation of at least one molecular scaffold in co-crystals with PYK2 kinase; identifying chemical structures of one or more of the molecular scaffolds that, when modified, alter the binding affinity or binding specificity or both between the molecular scaffold and the PYK2 kinase; synthesizing or otherwise obtaining a ligand in which one or more of the chemical structures of the molecular scaffold is modified to provide a ligand that binds to the PYK2 kinase with altered binding affinity or binding specificity or both. Thus, the invention provides a method for identifying or developing PYK2 ligands, *e.g.*, by identifying derivatives of PYK2 binding compounds, which may be molecular scaffolds, that have greater affinity and/or greater specificity for PYK2 than the parent compound. For example, the method can involve determining the binding orientation, identifying one or more chemical structures of one or more compounds that,when modified, alter the binding affinity and/or specificity; and synthesizing or otherwise obtaining a ligand in which one or more of those chemical structures is modified to provide a ligand that binds to PYK2 kinase with altered binding affinity or binding specificity or both. The method can also include identifying a molecular scaffold that binds to PYK2. Highly preferably the modified compound (ligand) also has altered activity (i.e., altered effect on the activity of PYK2 kinase).

[0029] The terms "PYK2 kinase" and "PYK2" mean an enzymatically active kinase that contains a portion at least 50 amino acid residues in length with greater than 90% amino acid sequence identity to at least a portion of PYK2 kinase domain (SEQ ID NO.: 1), for a

maximal alignment over an equal length segment; or that contains a portion with greater than 90% amino acid sequence identity to SEQ ID NO.: 1 that retains binding to ATP. Preferably the sequence identity is at least 95, 97, 98, 99, or even 100% with SEQ ID NO. 1. Preferably the identity is over a portion of SEQ ID NO: 1 that is at least 100, 150, 200, 250, or 272 amino acid in length.

[0030] The term "PYK2 kinase domain" refers to a reduced length PYK2 (*i.e.*, shorter than a full-length PYK2 by at least 100 amino acids at each of the N-terminus and the C-terminus) that includes the kinase catalytic region in PYK2, which is located near the center of the full-length molecule. Highly preferably for use in this invention, the kinase domain retains kinase activity, preferably at least 50% the level of kinase activity as compared to the native PYK2, more preferably at least 60, 70, 80, 90, or 100% of the native activity in a competitive kinase assay with ATP as a substrate and ATPγS as competitive inhibitor. An example is the PYK2 kinase domain of SEQ ID NO: 1.

[0031] As used herein, the terms "ligand" and "modulator" are used equivalently to refer to a compound that modulates the activity of a target biomolecule, *e.g.*, an enzyme such as a kinase. Generally a ligand or modulator will be a small molecule, where "small molecule refers to a compound with a molecular weight of 1500 daltons or less, or preferably 1000 daltons or less, 800 daltons or less, or 600 daltons or less. Thus, an "improved ligand" is one that possesses better pharmacological and/or pharmacokinetic properties than a reference compound, where "better" can be defined by a person for a particular biological system or therapeutic use. In terms of the development of ligands from scaffolds, a ligand is a derivative of a scaffold.

[0032] In the context of binding compounds, molecular scaffolds, and ligands, the term "derivative" or "derivative compound" refers to a compound having a chemical structure that contains a common core chemical structure as a parent or reference compound, but differs by having at least one structural difference, *e.g.*, by having one or more substituents added and/or removed and/or substituted, and/or by having one or more atoms substituted with different atoms. Unless clearly indicated to the contrary, the term "derivative" does not mean that the derivative is synthesized using the parent compound as a starting material or as an intermediate, although in some cases, the derivative may be synthesized from the parent.

[0033] Thus, the term "parent compound" refers to a reference compound for another compound, having structural features continued in the derivative compound. Often but not always, a parent compound has a simpler chemical structure than the derivative.

[0034] By "chemical structure" or "chemical substructure" is meant any definable atom or group of atoms that constitute a part of a molecule. Normally, chemical substructures of a scaffold or ligand can have a role in binding of the scaffold or ligand to a target molecule, or can influence the three-dimensional shape, electrostatic charge, and/or conformational properties of the scaffold or ligand.

[0035] The term "binds" in connection with the interaction between a target and a potential binding compound indicates that the potential binding compound preferentially associates with the target to a statistically significant degree as compared to association with proteins generally (*i.e.*, non-specific binding). Thus, the term "binding compound" refers to a compound that has such a statistically significant association with a target molecule. Preferably a binding compound interacts with a specified target with a dissociation constant (k_d) of 1 mM or less. A binding compound can bind with "low affinity", "very low affinity", "extremely low affinity", "moderate affinity", "moderately high affinity", or "high affinity" as described herein.

[0036] In the context of compounds binding to a target, the term "greater affinity" indicates that the compound binds more tightly than a reference compound, or than the same compound in a reference condition, *i.e.*, with a lower dissociation constant. In particular embodiments, the greater affinity is at least 2, 3, 4, 5, 8, 10, 50, 100, 200, 400, 500, 1000, or 10,000-fold greater affinity.

[0037] Also in the context of compounds binding to a biomolecular target, the term "greater specificity" indicates that a compound binds to a specified target to a greater extent than to another biomolecule or biomolecules that may be present under relevant binding conditions, where binding to such other biomolecules produces a different biological activity than binding to the specified target. Typically, the specificity is with reference to a limited set of other biomolecules, *e.g.*, in the case of PYK2, other kinases or even other type of enzymes. In particular embodiments, the greater specificity is at least 2, 3, 4, 5, 8, 10, 50, 100, 200, 400, 500, or 1000-fold greater specificity.

[0038] As used in connection with binding of a compound with PYK2, the term "interact" indicates that the distance from a bound compound to a particular amino acid residue will be 5.0 angstroms or less, or 6 angstroms or less with one water molecule coordinated between the compound and the residue, or 9 angstroms or less with two water molecules coordinated between the compound and the residue. In particular embodiments, the distance from the compound to the particular amino acid residue is 4.5 angstroms or less, 4.0 angstroms or less, or 3.5 angstroms or less. Such distances can be determined, for example, using co-crystallography, or estimated using computer fitting of a compound in a PYK2 active site.

[0039] Reference to particular amino acid residues in PYK2 polypeptide residue number is defined by the numbering provided in Lev et al. (1995) "Protein tyrosine kinase PYK2 involved in Ca(2+)-induced regulation of ion channel and MAP kinase functions" *Nature* 376:737-745.

[0040] In a related aspect, the invention provides a method for developing ligands specific for PYK2 kinase, where the method involves determining whether a derivative of a compound that binds to a plurality of kinases has greater specificity for the PYK2 kinase than the parent compound with respect to other kinases. In particular embodiments, the method also involves identifying such a compound that binds to a plurality of kinases.

[0041] As used herein in connection with binding compounds or ligands, the term "specific for PYK2 kinase", "specific for PYK2" and terms of like import mean that a particular compound binds to the particular PYK2 kinase to a statistically greater extent than to other kinases that may be present in a particular organism. Also, where biological activity other than binding is indicated, the term "specific for a PYK2 kinase" indicates that a particular compound has greater biological activity associated with binding PYK2 than to other kinases. Preferably, the specificity is also with respect to other biomolecules (not limited to kinases) that may be present from an organism.

[0042] In another aspect, the invention provides a method for obtaining improved ligands binding to PYK2, where the method involves identifying a compound that binds to PYK2, determining whether that compound interacts with one or more of PYK2 residues 503, 505, 457, 488, 567, and 554, and determining whether a derivative of that compound binds to the PYK2 kinase with greater affinity or greater specificity or both than the parent

binding compound. Binding with greater affinity or greater specificity or both than the parent compound indicates that the derivative is an improved ligand. This process can also be carried out in successive rounds of selection and derivatization and/or with multiple parent compounds to provide a compound or compounds with improved ligand characteristics. Likewise, the derivative compounds can be tested and selected to give high selectivity for the PYK2 kinase, or to give cross-reactivity to a particular set of targets, for example to a subset of kinases that includes PYK2. Certain compounds interact with the specified residues as 503, 505 (direct interacting), 457, 488, 567 (interact through 1 water), and 554 (interact through 2 waters). In particular embodiments, a molecular scaffold, binding compound, or ligand interacts with at least residues 503 and 505; residues 503 and 505 and at least one of residues 457, 488, and 567; at least residues 503, 505, 457, 488, and 567.

[0043] By "molecular scaffold" or "scaffold" is meant a simple target binding molecule to which one or more additional chemical moieties can be covalently attached, modified, or eliminated to form a plurality of molecules with common structural elements. The moieties can include, but are not limited to, a halogen atom, a hydroxyl group, a methyl group, a nitro group, a carboxyl group, or any other type of molecular group including, but not limited to, those recited in this application. Molecular scaffolds bind to at least one target molecule, preferably to a plurality of molecules in a target family, *e.g.*, a protein family. Preferred target molecules include enzymes and receptors, as well as other proteins. Preferred characteristics of a scaffold can include binding at a target molecule binding site such that one or more substituents on the scaffold are situated in binding pockets in the target molecule binding site; having chemically tractable structures that can be chemically modified, particularly by synthetic reactions, *e.g.*, so that a combinatorial library can be easily constructed; having chemical positions where moieties can be attached that do not interfere with binding of the scaffold to a protein binding site, such that the scaffold or library members can be modified to form ligands, to achieve additional desirable characteristics, *e.g.*, enabling the ligand to be actively transported into cells and/or to specific organs, or enabling the ligand to be attached to a chromatography column for additional analysis. Thus, a molecular scaffold is an identified target binding molecule prior to modification to improve binding affinity and/or specificity, or other pharmacalogic properties.

[0044] The term "scaffold core" refers to the core structure of a molecular scaffold onto which various substituents can be attached. Thus, for a number of scaffold molecules of a particular chemical class, the scaffold core is common to all the scaffold molecules. In many cases, the scaffold core will consist of or include one or more ring structures.

[0045] By "binding site" is meant an area of a target molecule to which a ligand can bind non-covalently. Binding sites embody particular shapes and often contain multiple binding pockets present within the binding site. The particular shapes are often conserved within a class of molecules, such as a protein family. Binding sites within a class also can contain conserved structures such as, for example, chemical moieties, the presence of a binding pocket, and/or an electrostatic charge at the binding site or some portion of the binding site, all of which can influence the shape of the binding site.

[0046] By "binding pocket" is meant a specific volume within a binding site. A binding pocket can often be a particular shape, indentation, or cavity in the binding site. Binding pockets can contain particular chemical groups or structures that are important in the non-covalent binding of another molecule such as, for example, groups that contribute to ionic, hydrogen bonding, or van der Waals interactions between the molecules.

[0047] By "orientation", in reference to a binding compound bound to a target molecule is meant the spatial relationship of the binding compound (which can be defined by reference to at least some of its consitituent atoms) to the binding site and/or atoms of the target molecule at least partially defining the binding site, typically including one or more binding pockets and/or atoms defining one or more binding pockets.

[0048] In the context of target molecules in this invention, the term "crystal" refers to a regular assemblage of a target molecule of a type suitable for X-ray crystallography. That is, the assemblage produces an X-ray diffraction pattern when illuminated with a beam of X-rays. Thus, a crystal is distinguished from an agglomeration or other complex of target molecule that does not give a diffraction pattern.

[0049] By "co-crystal" is meant a complex of the compound, molecular scaffold, or ligand bound non-covalently to the target molecule and present in a crystal form appropriate for analysis by X-ray or protein crystallography. In preferred embodiments the target molecule-ligand complex can be a protein-ligand complex.

[0050] The phrase "alter the binding affinity or binding specificity" refers to changing the binding constant of a first compound for another, and/or changing the level of binding of a first compound for a second compound as compared to the level of binding of the first compound for third compounds, respectively. For example, the binding specificity of a compound for a particular protein is increased if the relative level of binding to that particular protein is increased as compared to binding of the compound to unrelated proteins.

[0051] As used herein in connection with test compounds, binding compounds, and modulators (ligands), the term "synthesizing" and like terms means chemical synthesis from one or more precursor materials.

[0052] The phrase "chemical structure of the molecular scaffold is modified" means that a derivative molecule has a chemical structure that differs from that of the molecular scaffold but still contains common core chemical structural features. The phrase does not necessarily mean that the molecular scaffold is used as a precursor in the synthesis of the derivative.

[0053] By "assaying" is meant the creation of experimental conditions and the gathering of data regarding a particular result of the experimental conditions. For example, enzymes can be assayed based on their ability to act upon a detectable substrate. A compound or ligand can be assayed, for example, based on its ability to bind to a particular target molecule or molecules.

[0054] Certain compounds have been identified as molecular scaffolds and binding compounds for PYK2. Thus, in another aspect, the invention provides a method for identifying a ligand binding to PYK2, that includes determining whether a derivative compound that includes a core structure of Formula I as described herein binds to PYK2 with altered binding affinity or specificity or both as compared to a parent compound.

[0055] In reference to compounds of Formula I, the term "core structure" refers to the ring structure shown diagramatically as part of the description of compounds of Formula I, but excluding substituents. More generally, the term "core structure" refers to a characteristic chemical structure common to a set of compounds, especially a chemical structure than carries variable substituents in the compound set.

[0056] By a "set" of compounds is meant a collection of compounds. The compounds may or may not be structurally related.

[0057] In another aspect, structural information about PYK2 can also be used to assist in determining a struture for another kinase, *e.g.*, FAK, by creating a homology model from an electronic representation of a PYK2 structure.

[0058] Typically creating such a homology model involves identifying conserved amino acid residues between PYK2 and the other kinase of interest; transferring the atomic coordinates of a plurality of conserved amino acids in the PYK2 structure to the corresponding amino acids of the other kinase to provide a rough structure of that kinase; and constructing structures representing the remainder of the other kinase using electronic representations of the structures of the remaining amino acid residues in the other kinase. In particular, coordinates from Table 1 or Table 2 for conserved residues can be used. Conserved residues in a binding site, *e.g.*, PYK2 residues 503, 505, 457, 488, 567, and 554, can be used.

[0059] To assist in developing other portions of the kinase structure, the homology model can also utilize, or be fitted with, low resolution X-ray diffraction data from one or more crystals of the kinase, *e.g.*, to assist in linking conserved residues and/or to better specify coordinates for terminal portions of a polypeptide.

[0060] The PYK2 structural information used can be for a variety of different PYK2 variants, including full-length wild type, naturally-occurring variants (*e.g.*, allelic variants and splice variants), truncated variants of wild type or naturally-occuring variants, and mutants of full-length or truncated wild-type or naturally-occurring variants (that can be mutated at one or more sites). For example, in order to provide a PYK2 structure closer to a variety of other kinase structures, a mutated PYK2 that includes a mutation to a conserved residue in a binding site can be used (or a plurality of such mutations).

[0061] In another aspect, the invention provides a crystalline form of PYK2, which may be a reduced length PYK2 such as a PYK2 kinase domain, *e.g.*, having atomic coordinates as described in Table 1 or Table 2. The crystalline form can contain one or more heavy metal atoms, for example, atoms useful for X-ray crystallography. The crystalline form can also include a binding compound in a co-crystal, *e.g.*, a binding compound that

interacts with one more more of PYK2 residues residues 503, 505, 457, 488, 567, and 554 or any two, any three, any four, any five, or all six of those residues, and can, for example, be a compound of Formula I. PYK2 crystals can be in various environments, *e.g.*, in a crystallography plate, mounted for X-ray crystallography, and/or in an X-ray beam. The PYK2 may be of various forms, *e.g.*, a wild-type, variant, truncated, and/or mutated form as described herein.

[0062] The invention further concerns co-crystals of PYK2, which may a reduced length PYK2, *e.g.*, a PYK2 kinase domain, and a PYK2 binding compound. Advantageously, such co-crystals are of sufficient size and quality to allow structural determination of PYK2 to at least 3 Angstroms, 2.5 Angstroms, 2.0 Angstroms, or 1.8 Angstroms. The co-crystals can, for example, be in a crystallography plate, be mounted for X-ray crystallography and/or in an X-ray beam. Such co-crystals are beneficial, for example, for obtaining structural information concerning interaction between PYK2 and binding compounds.

[0063] PYK2 binding compounds can include compounds that interact with at least one of PYK2 residues 503, 505, 457, 488, 567, and 554, or any 2, 3, 4, 5, or all 6 of those residues. Exemplary compounds that bind to PYK2 include compounds of Formula I.

[0064] Likewise, in additional aspects, methods for obtaining PYK2 crystals and co-crystals are provided. In one aspect is provided a method for obtaining a crystal of PYK2 kinase domain, by subjecting PYK2 kinase domain protein at 5-20 mg/ml, preferably 8-12 mg/ml, to crystallization condition as described below, or conditions substantially equivalent thereto:

2-10 % (*e.g.*, 8%) polyethylene glycol (PEG) 8000, 0.2 M sodium acetate, 0.1% sodium cacodylate pH 6.5, 20% glycerol.

In general, the PYK2 will be in a solution containing the protein and suitable buffer. For example, the solution can contain 20 mM Tris-HCl ph 8.0, 150 mM NaCl, 14 mM β-mercaptoethanol (BME), and 1 mM dithiothreitol (DTT).

[0065] Crystallization conditions can be initially identified using a screening kit, such as a Hampton Research (Riverside, CA) screening kit 1 and/or 2. Conditions resulting in crystals can be selected and crystallization conditions optimized based on the demonstrated crystallization conditions. To assist in subsequent crystallography, the

PYK2 can be seleno-methionine labeled. Also, as indicated above, the PYK2 may be any of various forms, *e.g.*, truncated to provide a PYK2 kinase domain, which can be selected to be of various lengths.

[0066] In connection with chemical concentrations, the terms "approximately" and "about" mean ±20% of the indicated value.

[0067] In the context of crystallization conditions, the term "substantially equivalent" means conditions in a range around identified crystallization conditions such that the concentrations of solution components are within ±10% of the stated value, pH is ±1 pH unit, preferable ±0.5 pH unit, polymer, salt, and buffer substitutions may be made so long as one of ordinary skill in the art of protein crystallization would recognize the solution with the substituted component as being likely to also result in crystallization (though re-optimization may be useful). An example of such a substitution can be the substitution of a particular size PEG with a slightly smaller or larger PEG product, or a mixture of both a larger and a smaller PEG product.

[0068] A related aspect provides a method for obtaining co-crystals of PYK2, which can be a reduced length PYK2, with a binding compound, by subjecting PYK2 protein at 5-20 mg/ml to crystallization conditions substantially equivalent to the conditions as described above, in the presence of binding compound, for a time sufficient for cystal development. The binding compound may be added at various concentrations depending on the nature of the compound, *e.g.*, final concentration of 0.5 to 1.0 mM. In many cases, the binding compound will be in an organic solvent such as demethyl sulfoxide solution (DMSO). While not preferred, binding compound can also be soaked into a PYK2 crystal, *e.g.*, using conventional techniques.

[0069] In another aspect, provision of compounds active on PYK2 also provides a method for modulating PYK2 activity by contacting PYK2 with a compound that binds to PYK2 and interacts with one more of residues residues 503, 505, 457, 488, 567, and 554, for example a compound of Formula I. The compound is preferably provided at a level sufficient to modulate the activity of PYK2 by at least 10%, more preferably at least 20%, 30%, 40%, or 50%. In many embodiments, the compound will be at a concentration of about 1 μM, 100 μM, or 1 mM, or in a range of 1-100 nM, 100-500 nM, 500-1000 nM, 1-100 μM, 100-500 μM, or 500-1000 μM.

[0070] As used herein, the term "modulating" or "modulate" refers to an effect of altering a biological activity, especially a biological activity associated with a particular biomolecule such as PYK2. For example, an agonist or antagonist of a particular biomolecule modulates the activity of that biomolecule, *e.g.*, an enzyme.

[0071] The term "PYK2 activity" refers to a biological activity of PYK2, particularly including kinase activity.

[0072] In the context of the use, testing, or screening of compounds that are or may be modulators, the term "contacting" means that the compound(s) are caused to be in sufficient proximity to a particular molecule, complex, cell, tissue, organism, or other specified material that potential binding interactions and/or chemical reaction between the compound and other specified material can occur.

[0073] In a related aspect, the invention provides a method for treating a patient suffering from or at risk of a disease or condition for which modulation of PYK2 activity provides a therapeutic or prophylactic effect, *e.g.*, a disease or condition characterized by abnormal PYK2 kinase activity, where the method involves administering to the patient a compound that interacts with at least 2, or three or more of PYK2 residues residues 503, 505, 457, 488, 567, and 554 (*e.g.*, a compound of Formula I).

[0074] Specific diseases or disorders which might be treated or prevented cells include: myasthenia gravis; neuroblastoma; disorders caused by neuronal toxins such as cholera toxin, pertusis toxin, or snake venom; acute megakaryocytic myelosis; thrombocytopenia; those of the central nervous system such as seizures, stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage such as in cardiac arrest or neonatal distress, epilepsy, neurodegenerative diseases such as Alzheimer's disease, Huntington's disease and Parkinson's disease, dementia, muscle tension, depression, anxiety, panic disorder, obsessive-compulsive disorder, post-traumatic stress disor-der, schizophrenia, neuroleptic malignant syndrome, and Tourette's syndrome. Conditions that may be treated by PYK2 inhibitors include epilepsy, schizophrenia, extreme hyperactivity in children, chronic pain, and acute pain. Examples of conditions that may be treated by PYK2 enhancers (for example a phosphatase inhibitor) include stroke, Alzheimer's, Parkinson's, other neurodegenerative diseases, and migraine.

[0075] Preferred disorders include epilepsy, stroke, schizophrenia, and Parkinson's disorder, as there is a well established relationship between these disorders and the function of potassium channels.

[0076] In addition, PYK2 can act as a target for therapeutics for treating cell proliferative diseases. Thus, in certain embodiments, the disease or condition is a proliferative disease or neoplasia, such as benign or malignant tumors, psoriasis, leukemias (such as myeloblastic leukemia), lymphoma, prostate cancer, liver cancer, breast cancer, sarcoma, neuroblastima, Wilm's tumor, bladder cancer, thyroid cancer, neoplasias of the epithelialorigin such as mammacarcinoma, a cancer of hematopoietic cells, or a chronic inflammatory disease or condition, resulting, for example, from a persistent infection (e.g., tuberculosis, syphilis, fungal infection), from prolonged exposure to endogenous (e.g., elevated plasma lipids) or exogenous (e.g., silica, asbestos, cigarette tar, surgical sutures) toxins, and from autoimmune reactions (e.g., rheumatoid arthritis, systemic lupus erythrymatosis, multiple sclerosis, psoriasis). Thus, chronic inflammatory diseases include many common medical conditions, such as rheumatoid arthritis, restenosis, psoriasis, multiple sclerosis, surgical adhesions, tuberculosis, and chronic inflammatory lung and airway diseases, such as asthma pheumoconiosis, chronic obstructive pulmonary disease, nasal polyps, and pulmonary fibrosis. PYK2 modulators may also be useful in inhibiting development of hematomous plaque and restinosis, in controlling restinosis, as anti-metastatic agents, in treating diabetic complications, as immunosuppressants, and in control of angiogenesis to the extent a PYK2 kinase is involved in a particular disease or condition.

[0077] As crystals of PYK2 have been developed and analyzed, another aspect concerns an electronic representation of PYK2 (which may be a reduced length PYK2), for example, an electronic representation containing atomic coordinate representations corresponding to the coordinates listed for PYK2 in Table 1 or Table 2, or a schematic representation such as one showing secondary structure and/or chain folding, and may also show conserved active site residues. The PYK2 may be wild type, an allelic variant, a mutant form, or a modifed form, *e.g.*, as described herein.

[0078] The electronic representation can also be modified by replacing electronic representations of particular residues with electronic representations of other residues.

Thus, for example, an electronic representation containing atomic coordinate representations corresponding to the coordinates for PYK2 listed in Table 1 or Table 2 can be modified by the replacement of coordinates for a particular conserved residue in a binding site by a different amino acid. Likewise, a PYK2 representation can be modified by the respective substitutions, insertions, and/or deletions of amino acid residues to provide a representation of a structure for FAK kinase. Following a modification or modifications, the representation of the overall structure can be adjusted to allow for the known interactions that would be affected by the modification or modifications. In most cases, a modification involving more than one residue will be performed in an iterative manner.

[0079] In addition, an electronic representation of a PYK2 binding compound or a test compound in the binding site can be included, *e.g.*, a compound of Formula I.

[0080] Likewise, in a related aspect, the invention concerns an electronic representation of a portion of a PYK2 kinase, a binding site (which can be an active site) or kinase domain, for example, residues 419-691. A binding site or kinase domain can be represented in various ways, *e.g.*, as representations of atomic coordinates of residues around the binding site and/or as a binding site surface contour, and can include representations of the binding character of particular residues at the binding site, e.g., conserved residues. As for electronic representations of PYK2, a binding compound or test compound may be present in the binding site; the binding site may be of a wild type, variant, mutant form, or modified form of PYK2.

[0081] In yet another aspect, the structural information of PYK2 can be used in a homology model (based on PYK2) for another kinase (such as FAK), thus providing an electronic representation of a PYK2 based homology model for a kinase. For example, the homology model can utilize atomic coordinates from Table 1 for conserved amino acid residues. In particular embodiments; atomic coordinates for a wild type, variant, modified form, or mutated form of PYK2 can be used, including, for example, wild type, variants, modified forms, and mutant forms as described herein. In particular, PYK2 structure provides a very close homology model for FAK kinases. Thus, in particular embodiments the invention provides PYK2-based homology models of FAK.

[0082] In still another aspect, the invention provides an electronic representation of a modified PYK2 crystal structure, that includes an electronic representation of the atomic coordinates of a modified PYK2. In an exemplary embodiment, atomic coordinates of Table 1 or Table 2 can be modified by the replacement of atomic coordinates for a particular amino acid with atomic coordinates for a different amino acid. Modifications can include substitutions, deletions (e.g., C-terminal and/or N-terminal delections), insertions (internal, C-terminal, and/or N-terminal) and/or side chain modifications.

[0083] In another aspect, the PYK2 structural information provides a method for developing useful biological agents based on PYK2, by analyzing a PYK2 structure to identify at least one sub-structure for forming the biological agent. Such sub-structures can include epitopes for antibody formation, and the method includes developing antibodies against the epitopes, *e.g.*, by injecting an epitope presenting composition in a mammal such as a rabbit, guinea pig, pig, goat, or horse. The sub-structure can also include a mutation site at which mutation is expected to or is known to alter the activity of the PYK2, and the method includes creating a mutation at that site. Still further, the sub-structure can include an attachment point for attaching a separate moiety, for example, a peptide, a polypeptide, a solid phase material (*e.g.*, beads, gels, chromatographic media, slides, chips, plates, and well surfaces), a linker, and a label (*e.g.*, a direct label such as a fluorophore or an indirect label, such as biotin or other member of a specific binding pair). The method can include attaching the separate moiety.

[0084] In another aspect, the invention provides a method for identifying potential PYK2, binding compounds by fitting at least one electronic representation of a compound in an electronic representation of a PYK2 binding site. The representation of the binding site may be part of an electronic representation of a larger portion(s) or all of a PYK2 molecule or may be a representation of only the binding site or active site. The electronic representation may be as described above or otherwise described herein.

[0085] In particular embodiments, the method involves fitting a computer representation of a compound from a computer database with a computer representation of the active site of a PYK2 kinase, and involves removing a computer representation of a compound complexed with the PYK2 molecule and identifying compounds that best fit the active site

based on favorable geometric fit and energetically favorable complementary interactions as potential binding compounds.

[0086] In other embodiments, the method involves modifying a computer representation of a compound complexed with a PYK2 molecule, by the deletion or addition or both of one or more chemical groups; fitting a computer representation of a compound from a computer database with a computer representation of the active site of the PYK2 molecule; and identifying compounds that best fit the active site based on favorable geometric fit and energetically favorable complementary interactions as potential binding compounds.

[0087] In still other embodiments, the method involves removing a computer representation of a compound complexed with a PYK2 kinase, and searching a database for compounds having structural similarity to the complexed compound using a compound searching computer program or replacing portions of the complexed compound with similar chemical structures using a compound construction computer program.

[0088] Fitting a compound can include determining whether a compound will interact with one or more of PYK2 residues residues 503, 505, 457, 488, 567, and 554. Compounds selected for fitting or that are complexed with PYK2 can, for example, be compounds of Formula I.

[0089] In another aspect, the invention concerns a method for attaching a PYK2 kinase binding compound to an attachment component, as well as a method for indentifying attachment sites on a PYK2 kinase binding compound. The method involves identifying energetically allowed sites for attachment of an attachment component for the binding compound bound to a binding site of PYK2; and attaching the compound or a derivative thereof to the attachment component at the energetically allowed site.

[0090] As used in connection with binding compounds, an "attachment component" refers to a moiety that is attached to a binding compound for adding a functionality other than binding with the target molecule and that does not prevent such binding. Examples include direct and indirect labels, linkers, and hapten and other specific recognition moieties. Linkers (including traceless linkers) can be incorporated, for example, for attachment to a solid phase or to another molecule or other moiety. Such attachment can

be formed by synthesizing the compound or derivative on the linker attached to a solid phase medium e.g., in a combinatorial synthesis in a plurality of compound. Likewise, the attachment to a solid phase medium can provide an affinity medium (e.g., for affinity chromatography). Labels can be a directly detectable label such as a fluorophore, or an indirectly detectable such as a member of a specific binding pair, *e.g.*, biotin.

[0091] The ability to identify energentically allowed sites on a PYK2 kinase binding compound also, in a related aspect, provides modified binding compounds that have linkers attached, for example, compounds of Formula I, preferably at an energetically allowed site for binding of the modified compound to PYK2. The linker can be attached to an attachment component as described above.

[0092] Another aspect concerns a modified PYK2 polypeptide that includes a modification that makes the modified PYK2 more similar than native PYK2 to another kinase, and can also include other mutations or other modifications. In various embodiments, the polypeptide includes a full-length PYK2 polypeptide, includes a modified PYK2 binding site, includes at least 20, 30, 40, 50, 60, 70, or 80 contiguous amino acid residues derived from PYK2 including a conserved site.

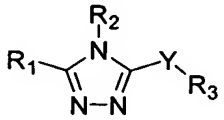
[0093] Still another aspect of the invention concerns a method for developing a ligand for a kinase that includes conserved residues matching any one, 2, 3, 4, 5, or 6 of PYK2 residues 503, 505, 457, 488, 567, and 554, by determining whether a compound of Formula I binds to the kinase. The method can also include determining whether the compound modulates the activity of the kinase. Preferably the kinase has at least 50, 55, 60, or 70% identity over an equal length kinase domain segment.

[0094] In particular embodiments, the determining includes computer fitting the compound in a binding site of the kinase and/or the method includes forming a co-crystal of the kinase and the compound. Such co-crystals can be used for determing the binding orientation of the compound with the kinase and/or provide structural information on the kinase, e.g., on the binding site and interacting amino acid residues. Such binding orientation and/or other structural information can be accomplished using X-ray crystallography.

[0095] Reference to "matching" of a specified conserved amino acid residue in a kinase domain means that in a maximal alignment of the amino acid sequences of that kinase domain with a different kinase domain, there is an amino acid residue aligned with the specified residue that is either the same amino acid or represents a conservative substitution. Preferably, the matching amino acid residue is within 5 angstroms rms in an overlay of crystal structure atomic coordinates for backbone atoms.

[0096] The invention also provides compounds that bind to and/or modulate (*e.g.*, inhibit) PYK2, *e.g.*, PYK2 kinase activity. Accordingly, in aspects and embodiments involving PYK2 binding compounds, molecular scaffolds, and ligands or modulators, the compound is a weak binding compound; a moderate binding compound; a strong binding compound; the compound interacts with one or more of PYK2 residues 503, 505, 457, 488, 567, and 554; the compound is a small molecule; the compound binds to a plurality of different kinases (*e.g.*, at least 3, 5, 10, 15, 20 different kinases). In particular embodiments, the invention concerns compounds of Formula I, as described below.

[0097] Thus, in certain embodiments, the invention concerns compounds of Formula I:



Formula I

where:

[0098] R^1 is hydrogen, trifluormethyl, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, or N $R^{16}R^{17}$;

[0099] R^2 is hydrogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl,

optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-C(X)R^{20}$, $C(X)NR^{16}R^{17}$, or $-S(O_2)R^{21}$;

[0100] R^3 is hydrogen, trifluoromethyl, optionally substituted alkoxyl, optionally substituted thioalkoxy, optionally substituted amine, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

[0101] R^{16} and R^{17} are independently hydrogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl;

[0102] R^{20} is hydroxyl, optionally substituted lower alkoxy, optionally substituted amine, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

[0103] R^{21} is optionally substituted lower alkoxy, optionally substituted amine, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl;

[0104] X = O, or S.

[0105] Y = S, O, $NR^{16}R^{17}$, $-C(X)R^{20}$, or optionally substituted alkyl.

[0106] In Formula I and the descriptions of substituents, subscripts and superscripts are to be regarded as equivalent.

[0107] In certain embodiments involving compounds of Formula I, X and Y are O; X is O and Y is S; X is O and Y is $NR^{16}R^{17}$; X is O and Y is $-C(X)R^{20}$; X is S and Y is O; X is S and Y is S; X is S and Y is and Y is $NR^{16}R^{17}$; X is S and Y is $-C(X)R^{20}$.

[0108] In certain embodiments, X = O, Y = O, and R^1 is hydrogen; X = O, Y = O, and R^2 is hydrogen; X = O, Y = S, and R^1 is hydrogen; X = O, Y = S, and R^2 is hydrogen; X = O, Y = N $R^{16}R^{17}$, and R^1 is hydrogen; X = O, Y = S, and R^2 is hydrogen; X = O, Y = N $R^{16}R^{17}$, and R^2 is hydrogen; X = O, Y = $-C(X)R^{20}$, and R^1 is hydrogen; X = O, Y = $-C(X)R^{20}$, and R^2 is hydrogen; X = O, Y = optionally substituted alkyl, and R^1 is hydrogen; X = O, Y = optionally substituted alkyl, and R^2 is hydrogen.

[0109] In certain embodiments, X = S, Y = O, and R^1 is hydrogen; X = S, Y = O, and R^2 is hydrogen; X = S, Y = S, and R^1 is hydrogen; X = S, Y = S, and R^2 is hydrogen; X = S, Y = N $R^{16}R^{17}$, and R^1 is hydrogen; X = S, Y = S, and R^2 is hydrogen; X = S, Y = N $R^{16}R^{17}$, and R^2 is hydrogen; X = S, Y = $-C(X)R^{20}$, and R^1 is hydrogen; X = S, Y = $-C(X)R^{20}$, and R^2 is hydrogen; X = S, Y = optionally substituted alkyl, and R^1 is hydrogen; X = S, Y = optionally substituted alkyl, and R^2 is hydrogen.

[0110] In certain embodiments, R^1 is hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, or N $R^{16}R^{17}$.

[0111] In certain embodiments, R^2 is hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, $C(X)NR^{16}R^{17}$, or $-S(O_2)R^{21}$.

[0112] An additional aspect of this invention relates to pharmaceutical formulations, that include a therapeutically effective amount of a compound of Formula I and at least one pharmaceutically acceptable carrier or excipient. The composition can include a plurality of different pharmacalogically active compounds.

[0113] "Halo" or "Halogen" - alone or in combination means all halogens, that is, chloro (Cl), fluoro (F), bromo (Br), iodo (I).

[0114] "Hydroxyl" refers to the group -OH.

[0115] "Thiol" or "mercapto" refers to the group -SH.

[0116] "Alkyl" - alone or in combination means an alkane-derived radical containing from 1 to 20, preferably 1 to 15, carbon atoms (unless specifically defined). It is a straight chain alkyl, branched alkyl or cycloalkyl. Preferably, straight or branched alkyl groups containing from 1-15, more preferably 1 to 8, even more preferably 1-6, yet more preferably 1-4 and most preferably 1-2, carbon atoms, such as methyl, ethyl, propyl, isopropyl, butyl, t-butyl and the like. The term "lower alkyl" is used herein to describe the straight chain alkyl groups described immediately above. Preferably, cycloalkyl groups are monocyclic, bicyclic or tricyclic ring systems of 3-8, more preferably 3-6, ring members per ring, such as cyclopropyl, cyclopentyl, cyclohexyl, adamantyl and the like. Alkyl also includes a straight chain or branched alkyl group that contains or is interrupted by a cycloalkyl portion. The straight chain or branched alkyl group is attached at any available point to produce a stable compound. Examples of this include, but are not limited to, 4-(isopropyl)-cyclohexylethyl or 2-methyl-cyclopropylpentyl. A substituted alkyl is a straight chain alkyl, branched alkyl, or cycloalkyl group defined previously, independently substituted with 1 to 3 groups or substituents of halo, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, acyloxy, aryloxy, heteroaryloxy, amino optionally mono- or di-substituted with alkyl, aryl or heteroaryl groups, amidino, urea optionally substituted with alkyl, aryl, heteroaryl or heterocyclyl groups, aminosulfonyl optionally N-mono- or N,N-di-substituted with alkyl, aryl or heteroaryl groups, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, or the like.

[0117] "Alkenyl" - alone or in combination means a straight, branched, or cyclic hydrocarbon containing 2-20, preferably 2-17, more preferably 2-10, even more preferably 2-8, most preferably 2-4, carbon atoms and at least one, preferably 1-3, more preferably 1-2, most preferably one, carbon to carbon double bond. In the case of a cycloalkyl group, conjugation of more than one carbon to carbon double bond is not such as to confer aromaticity to the ring. Carbon to carbon double bonds may be either contained within a cycloalkyl portion, with the exception of cyclopropyl, or within a straight chain or branched portion. Examples of alkenyl groups include ethenyl, propenyl, isopropenyl, butenyl, cyclohexenyl, cyclohexenylalkyl and the like. A substituted alkenyl is the straight chain alkenyl, branched alkenyl or cycloalkenyl group defined previously, independently substituted with 1 to 3 groups or substituents of halo, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, acyloxy, aryloxy, heteroaryloxy, amino optionally

mono- or di-substituted with alkyl, aryl or heteroaryl groups, amidino, urea optionally substituted with alkyl, aryl, heteroaryl or heterocyclyl groups, aminosulfonyl optionally N-mono- or N,N-di-substituted with alkyl, aryl or heteroaryl groups, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, carboxy, alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, or the like attached at any available point to produce a stable compound.

[0118] "Alkynyl" - alone or in combination means a straight or branched hydrocarbon containing 2-20, preferably 2-17, more preferably 2-10, even more preferably 2-8, most preferably 2-4, carbon atoms containing at least one, preferably one, carbon to carbon triple bond. Examples of alkynyl groups include ethynyl, propynyl, butynyl and the like. A substituted alkynyl refers to the straight chain alkynyl or branched alkenyl defined previously, independently substituted with 1 to 3 groups or substituents of halo, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, acyloxy, aryloxy, heteroaryloxy, amino optionally mono- or di-substituted with alkyl, aryl or heteroaryl groups, amidino, urea optionally substituted with alkyl, aryl, heteroaryl or heterocyclyl groups, aminosulfonyl optionally N-mono- or N,N-di-substituted with alkyl, aryl or heteroaryl groups, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, or the like attached at any available point to produce a stable compound.

[0119] "Alkyl alkenyl" refers to a group -R-CR'=CR''' R'''', where R is lower alkyl, or substituted lower alkyl, R', R''', R'''' may independently be hydrogen, halogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, hetaryl, or substituted hetaryl as defined below.

[0120] "Alkyl alkynyl" refers to a groups -RCCR' where R is lower alkyl or substituted lower alkyl, R' is hydrogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, hetaryl, or substituted hetaryl as defined below.

[0121] "Alkoxy" denotes the group -OR, where R is lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroalkyl, heteroarylalkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, or substituted cycloheteroalkyl as defined.

[0122] "Alkylthio" or "thioalkoxy" denotes the group -SR, $-S(O)_{n=1-2}-R$, where R is lower alkyl, substituted lower alkyl, aryl, substituted aryl, aralkyl or substituted aralkyl as defined herein.

[0123] "Acyl" denotes groups -C(O)R, where R is hydrogen, lower alkyl substituted lower alkyl, aryl, substituted aryl and the like as defined herein.

[0124] "Aryloxy" denotes groups -OAr, where Ar is an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group as defined herein.

[0125] "Amino" or substituted amine denotes the group NRR', where R and R' may independently by hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, hetaryl, or substituted heteroaryl as defined herein, acyl or sulfonyl.

[0126] "Amido" denotes the group -C(O)NRR', where R and R' may independently by hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, hetaryl, substituted hetaryl as defined herein.

[0127] "Carboxyl" denotes the group -C(O)OR, where R is hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, hetaryl, and substituted hetaryl as defined herein.

[0128] "Aryl" - alone or in combination means phenyl or naphthyl optionally carbocyclic fused with a cycloalkyl of preferably 5-7, more preferably 5-6, ring members and/or optionally substituted with 1 to 3 groups or substituents of halo, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, acyloxy, aryloxy, heteroaryloxy, amino optionally mono- or di-substituted with alkyl, aryl or heteroaryl groups, amidino, urea optionally substituted with alkyl, aryl, heteroaryl or heterocyclyl groups, aminosulfonyl optionally N-mono- or N,N-di-substituted with alkyl, aryl or heteroaryl groups, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, or the like.

[0129] "Substituted aryl" refers to aryl optionally substituted with one or more functional groups, e.g., halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, thiol, sulfamido and the like.

[0130] "Heterocycle" refers to a saturated, unsaturated, or aromatic carbocyclic group having a single ring (e.g., morpholino, pyridyl or furyl) or multiple condensed rings (e.g., naphthpyridyl, quinoxalyl, quinolinyl, indolizinyl or benzo[b]thienyl) and having at least one hetero atom, such as N, O or S, within the ring, which can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0131] "Heteroaryl" - alone or in combination means a monocyclic aromatic ring structure containing 5 or 6 ring atoms, or a bicyclic aromatic group having 8 to 10 atoms, containing one or more, preferably 1-4, more preferably 1-3, even more preferably 1-2, heteroatoms independently selected from the group O, S, and N, and optionally substituted with 1 to 3 groups or substituents of halo, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, acyloxy, aryloxy, heteroaryloxy, amino optionally mono- or di-substituted with alkyl, aryl or heteroaryl groups, amidino, urea optionally substituted with alkyl, aryl, heteroaryl or heterocyclyl groups, aminosulfonyl optionally N-mono- or N,N-di-substituted with alkyl, aryl or heteroaryl groups, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, or the like. Heteroaryl is also intended to include oxidized S or N, such as sulfinyl, sulfonyl and N-oxide of a tertiary ring nitrogen. A carbon or nitrogen atom is the point of attachment of the heteroaryl ring structure such that a stable aromatic ring is retained. Examples of heteroaryl groups are pyridinyl, pyridazinyl, pyrazinyl, quinazolinyl, purinyl, indolyl, quinolinyl, pyrimidinyl, pyrrolyl, oxazolyl, thiazolyl, thienyl, isoxazolyl, oxathiadiazolyl, isothiazolyl, tetrazolyl, imidazolyl, triazinyl, furanyl, benzofuryl, indolyl and the like. A substituted heteroaryl contains a substituent attached at an available carbon or nitrogen to produce a stable compound.

[0132] "Heterocyclyl" - alone or in combination means a non-aromatic cycloalkyl group having from 5 to 10 atoms in which from 1 to 3 carbon atoms in the ring are replaced by heteroatoms of O, S or N, and are optionally benzo fused or fused heteroaryl of 5-6 ring members and/or are optionally substituted as in the case of cycloalkyl. Heterocycyl is also intended to include oxidized S or N, such as sulfinyl, sulfonyl and N-oxide of a tertiary ring nitrogen. The point of attachment is at a carbon or nitrogen atom. Examples of heterocyclyl groups are tetrahydrofuranyl, dihydropyridinyl, piperidinyl, pyrrolidinyl,

piperazinyl, dihydrobenzofuryl, dihydroindolyl, and the like. A substituted hetercyclyl contains a substituent nitrogen attached at an available carbon or nitrogen to produce a stable compound.

[0133] "Substituted heteroaryl" refers to a heterocycle optionally mono or poly substituted with one or more functional groups, e.g., halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0134] "Aralkyl" refers to the group -R-Ar where Ar is an aryl group and R is lower alkyl or substituted lower alkyl group. Aryl groups can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0135] "Heteroalkyl" refers to the group -R-Het where Het is a heterocycle group and R is a lower alkyl group. Heteroalkyl groups can optionally be unsubstituted or substituted with e.g., halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0136] "Heteroarylalkyl" refers to the group -R-HetAr where HetAr is an heteroaryl group and R lower alkyl or substituted lower alkyl. Heteroarylalkyl groups can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, substituted lower alkyl, alkoxy, alkylthio, acetylene, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0137] "Cycloalkyl" refers to a divalent cyclic or polycyclic alkyl group containing 3 to 15 carbon atoms.

[0138] "Substituted cycloalkyl" refers to a cycloalkyl group comprising one or more substituents with, e.g., halogen, lower alkyl, substituted lower alkyl, alkoxy, alkylthio, acetylene, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0139] "Cycloheteroalkyl" refers to a cycloalkyl group wherein one or more of the ring carbon atoms is replaced with a heteroatom (e.g., N, O, S or P).

[0140] "Substituted cycloheteroalkyl" refers to a cycloheteroalkyl group as herein defined which contains one or more substituents, such as halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0141] "Alkyl cycloalkyl" denotes the group -R-cycloalkyl where cycloalkyl is a cycloalkyl group and R is a lower alkyl or substituted lower alkyl. Cycloalkyl groups can optionally be unsubstituted or substituted with e.g. halogen, lower alkyl, lower alkoxy, alkylthio, acetylene, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0142] "Alkyl cycloheteroalkyl" denotes the group -R-cycloheteroalkyl where R is a lower alkyl or substituted lower alkyl. Cycloheteroalkyl groups can optionally be unsubstituted or substituted with e.g. halogen, lower alkyl, lower alkoxy, alkylthio, amino, amido, carboxyl, acetylene, hydroxyl, aryl, aryloxy, heterocycle, substituted heterocycle, hetaryl, substituted hetaryl, nitro, cyano, thiol, sulfamido and the like.

[0143] In addition to compounds (including molecular scaffolds) of Formula I as described herein, additional types of compounds can be used as modulators (e.g., inhibitors) of PYK2, and for development of further PYK2 ligands. In particular, compounds of the types described in Bremer et al., U.S. Application 10/664,421, filed September 16, 2003, and Bremer et al., U.S. Application 60/503,277, filed September 15, 2003, both of which are incorporated herein in their entireties, including drawings.

[0144] An additional aspect of this invention relates to pharmaceutical formulations, that include a therapeutically effective amount of a compound of Formula I, and at least one pharmaceutically acceptable carrier or excipient. The composition can include a plurality of different pharmacalogically active compounds.

[0145] Additional aspects and embodiments will be apparent from the following Detailed Description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0146] FIGURE 1 shows a ribbon diagram schematic representation of PYK2 active site.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0147] The Tables will first be briefly described.

[0148] Table 1 provides atomic coordinates for human PYK2 kinase domain. In this table and in Table 2, the various columns in the lines beginning with "ATOM" have the following content, beginning with the left-most column:
ATOM: Refers to the relevant moiety for the table row.
Atom number: Refers to the arbitrary atom number designation within the coordinate table.
Atom Name: Identifier for the atom present at the particular coordinates.
Chain ID: Chain ID refers to one monomer of the protein in the crystal, *e.g.*, chain "A", or to other compound present in the crystal, e.g., HOH for water, and L for a ligand or binding compound. Multiple copies of the protein monomers will have different chain Ids.
Residue Number: The amino acid residue number in the chain.
X, Y, Z: Respectively are the X, Y, and Z coordinate values.
Occupancy: Describes the fraction of time the atom is observed in the crystal. For example, occupancy = 1 means that the atom is present all the time; occupancy = o.5 indicates that the atom is present in the location 50% of the time.
B-factor: A measure of the thermal motion of the atom.
Element: Identifier for the element.

[0149] In addition, the lines that begin with "ANISOU" present the anisotropic temperature factors. The anisotropic temperture factors are related to the corresponding isotropic temperature factors (B-factors) in the "ATOM" lines in the table. Following "ANISOU", the next 4 entries are "Atom number", "Atom name", Residue name", and "Residue number", and are the same as the respective corresponding "ATOM" line entries. The next 6 entries are the anisotropic temperature factors U(1,1), U(2,2), U(3,3), U1,2), U(1,3), and U(2,3) in order (scaled by a factor of 10^4 (Angstroms^2) and presented as integers).

[0150] Table 2 provides atomic coordinates for PYK2 with (5'-adenylylimidodiphosphate) AMPPNP in the binding site.

[0151] Table 3 provides an alignment of kinase domains for several kinases, including human PYK2, providing identification of residues conserved between various members of the set. The residue number is for PYK2.

[0152] Table 4 provides the nucleic acid and amino acid sequences for human PYK2 kinase domain.

[0153] Table 5 provides representative assay results for kinase activity of PYK2 kinase domain in the presence of ATP and in the presence of several ATP analogs.

I. Introduction

[0154] The present invention concerns the use of PYK2 kinase structures, structural information, and related compositions for identifying compounds that modulate PYK2 kinase activity and for determining structuctures of other kinases.

[0155] PYK2 kinase is involved in a number of disease conditions. For example, as indicated in the Background above, PYK2 functions as a neurotransmitter regulator, and thus modulation of PYK2 can enhance or inhibit such signaling. In addition, due to the involve ment of PYK2 in linking the G protein-coupled pathway with the sos/grb pathway for MAP kinase signal tranduction activation. This may involve the binding of src. Thus, PYK2 can also affect cell proliferation.

Exemplary Diseases Associated with PYK2.

[0156] As indicated above, modulation of PYK2 activity is beneficial for treatment or prevention of a variety of diseases and conditions, such as those relating to its roles in signal transduction. As a result, PYK2 inhibitors have therapeutic applications in the treatment of proliferative diseases, such as various cancers, osteoporosis, and inflammation, as well as other disease states, such as those referenced in the Summary above and those otherwise indicated herein. PYK2, sceening for PYK2 modulators, and methods for using PYK2 modulators, along with related assays, techniques, and data, are described, for example, in Duong et al., PCT Application No. PCT/US98/02792, PCT Publication WO/98/35056; Schlessinger et al., PCT Application No. PCT/US98/27871,

PCT Publication WO 00/40971; Lev, et al., PCT Application PCT/US97/22565, PCT Publication WO 98/26054; Lev et al., PCT Application PCT/US95/15846, PCT Publication WO 96/18738, which are incorporated herein in their entireties.

Osteoporosis

[0157] Activation of osteoclasts is initiated by adhesion of osteoclast to bone surface. Cytoskeletal rearrangement results in formation of a sealing zone and a polarized ruffled membrane. Pyk2 was found to be highly expressed in osteoclasts. (Duong et al. (1998) "Pyk2 in osteoclasts is an adhesion kinase, localized in the sealing zone, activated by ligation of alpha(v)beta3 integrin, and phosphorylated by Src kinase." *J. Clin. Invest.* 102:881-892.) Studies indicate that Pyk2 is involved in the adhesion-induced formation of the sealing zone and is required for osteoclast bone resorption. (Duong and Rodan (1998) Integrin-mediated signaling in the regulation of osteoclast adhesion and activation." *Front. Biosci.* 3:757-768.)

Proliferative Diseases

[0158] In another example, modulation of PYK2 has been indicated for treatment of proliferative diseases such as cancer, e.g., for cancers of hematopoietic cells, among others. (Avraham et al., PCT Publication 98/07870, which is incorporated herein by reference in its entirety.)

Inflammation

[0159] Modulation of PYK2 has also been linked with treatment of inflammatory response-related diseases, generally those that have an aberrent inflammatory response, for example, inflammatory bowel diseases such as ulcerative colitis and Crohn's Disease, and connective tissue diseases such as rheumatoid arthritis, system lupus erythrmatosus, progressive systemin sclerosis, mixed connective tissue disease, and Sjogren's syndrome. (Schlessinger et al., PCT Publication WO 00/40971, which is incorporated herein by refernce in its entirety.) A pathologic inflammatory response may be a continuation of an acute inflammatory response, or a prolonged low-grade inflammatory response, and typically results in tissue damage. Macrophage and T-cell recruitment, and process such as cytokine production can directly contribute to inflammatory pathogenesis.

II. Crystalline PYK2 Kinase

[0160] Crystalline PYK2 kinases (*e.g.*, human PYK2) include native crystals, kinase domain crystals, derivative crystals, and co-crystals. The crystals generally comprise substantially pure polypeptides corresponding to the PYK2 kinase polyeptide in crystalline form. In connection with the development of inhibitors of PYK2 kinase function, it is advantageous to use PYK2 kinase domain for structural determination, because use of the reduced sequence simplifies structure determination. To be useful for this purpose, the kinase domain should be active and/or retain native-type binding, thus indicating that the kinase domain takes on substantially normal 3D structure.

[0161] It is to be understood that the crystalline kinases and kinase domains useful in the the invention are not limited to naturally occurring or native kinase. Indeed, the crystals include crystals of mutants of native kinases. Mutants of native kinases are obtained by replacing at least one amino acid residue in a native kinase with a different amino acid residue, or by adding or deleting amino acid residues within the native polypeptide or at the N- or C-terminus of the native polypeptide, and have substantially the same three-dimensional structure as the native kinase from which the mutant is derived.

[0162] By having substantially the same three-dimensional structure is meant having a set of atomic structure coordinates that have a root-mean-square deviation of less than or equal to about 2Å when superimposed with the atomic structure coordinates of the native kinase from which the mutant is derived when at least about 50% to 100% of the Cα atoms of the native kinase or kinase domain are included in the superposition.

[0163] Amino acid substitutions, deletions and additions which do not significantly interfere with the three-dimensional structure of the kinase will depend, in part, on the region of the kinase where the substitution, addition or deletion occurs. In highly variable regions of the molecule, non-conservative substitutions as well as conservative substitutions may be tolerated without significantly disrupting the three-dimensional, structure of the molecule. In highly conserved regions, or regions containing significant secondary structure, conservative amino acid substitutions are preferred. Such conserved and variable regions can be identified by sequence alignment of PYK2 with other kinases. Such alignment of PYK2 kinase domain along with a number of other kinase domains is provided in **Table 3**.

[0164] Conservative amino acid substitutions are well known in the art, and include substitutions made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the amino acid residues involved. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; amino acids with uncharged polar head groups having similar hydrophilicity values include the following: leucine, isoleucine, valine; glycine, alanine; asparagine, glutamine; serine, threonine; phenylalanine, tyrosine. Other conservative amino acid substitutions are well known in the art.

[0165] For kinases obtained in whole or in part by chemical synthesis, the selection of amino acids available for substitution or addition is not limited to the genetically encoded amino acids. Indeed, the mutants described herein may contain non-genetically encoded amino acids. Conservative amino acid substitutions for many of the commonly known non-genetically encoded amino acids are well known in the art. Conservative substitutions for other amino acids can be determined based on their physical properties as compared to the properties of the genetically encoded amino acids.

[0166] In some instances, it may be particularly advantageous or convenient to substitute, delete and/or add amino acid residues to a native kinase in order to provide convenient cloning sites in cDNA encoding the polypeptide, to aid in purification of the polypeptide, and for crystallization of the polypeptide. Such substitutions, deletions and/or additions which do not substantially alter the three dimensional structure of the native kinase domain will be apparent to those of ordinary skill in the art.

[0167] It should be noted that the mutants contemplated herein need not all exhibit kinase activity. Indeed, amino acid substitutions, additions or deletions that interfere with the kinase activity but which do not significantly alter the three-dimensional structure of the domain are specifically contemplated by the invention. Such crystalline polypeptides, or the atomic structure coordinates obtained therefrom, can be used to identify compounds that bind to the native domain. These compounds can affect the activity of the native domain.

[0168] The derivative crystals of the invention can comprise a crystalline kinase polypeptide in covalent association with one or more heavy metal atoms. The polypeptide

may correspond to a native or a mutated kinase. Heavy metal atoms useful for providing derivative crystals include, by way of example and not limitation, gold, mercury, selenium, etc.

[0169] The co-crystals of the invention generally comprise a crystalline kinase domain polypeptide in association with one or more compounds. The association may be covalent or non-covalent. Such compounds include, but are not limited to, cofactors, substrates, substrate analogues, inhibitors, allosteric effectors, etc.

[0170] Exemplary mutations for PYK2 family kinases include the insertion of a sequence having the FAK sequence shown in the Figure 3 alignment between PYK2 residues 482 and 483. Such insertion is useful, for example, to assist in using PYK2 kinases to model FAK kinase. Mutations at other sites can likewise be carried out, *e.g.*, to make a mutated PYK2 kinase more similar to another kinase for structure modeling and/or compound fitting purposes, such as a kinase in the kinase domain alignment in Table 3.

III. Three Dimensional Structure Determination Using X-ray Crystallography

[0171] X-ray crystallography is a method of solving the three dimensional structures of molecules. The structure of a molecule is calculated from X-ray diffraction patterns using a crystal as a diffraction grating. Three dimensional structures of protein molecules arise from crystals grown from a concentrated aqueous solution of that protein. The process of X-ray crystallography can include the following steps:

(a) synthesizing and isolating (or otherwise obtaining) a polypeptide;

(b) growing a crystal from an aqueous solution comprising the polypeptide with or without a modulator; and

(c) collecting X-ray diffraction patterns from the crystals, determining unit cell dimensions and symmetry, determining electron density, fitting the amino acid sequence of the polypeptide to the electron density, and refining the structure.

Production of Polypeptides

[0172] The native and mutated kinase polypeptides described herein may be chemically synthesized in whole or part using techniques that are well-known in the art (*see, e.g.*, Creighton (1983) *Biopolymers* 22(1):49-58).

[0173] Alternatively, methods which are well known to those skilled in the art can be used to construct expression vectors containing the native or mutated kinase polypeptide coding sequence and appropriate transcriptional/translational control signals. These methods include *in vitro* recombinant DNA techniques, synthetic techniques and *in vivo* recombination/genetic recombination. See, for example, the techniques described in Maniatis, T (1989). Molecular cloning: A laboratory Manual. Cold Spring Harbor Laboratory, New York. Cold Spring Harbor Laboratory Press; and Ausubel, F.M. et al. (1994) Current Protocols in Molecular Biology. John Wiley & Sons, Secaucus, N.J.

[0174] A variety of host-expression vector systems may be utilized to express the kinase coding sequence. These include but are not limited to microorganisms such as bacteria transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing the kinase domain coding sequence; yeast transformed with recombinant yeast expression vectors containing the kinase domain coding sequence; insect cell systems infected with recombinant virus expression vectors (*e.g.*, baculovirus) containing the kinase domain coding sequence; plant cell systems infected with recombinant virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.*, Ti plasmid) containing the kinase domain coding sequence; or animal cell systems. The expression elements of these systems vary in their strength and specificities.

[0175] Depending on the host/vector system utilized, any of a number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used in the expression vector. For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage λ, plac, ptrp, ptac (ptrp-lac hybrid promoter) and the like may be used; when cloning in insect cell systems, promoters such as the baculovirus polyhedrin promoter may be used; when cloning in plant cell systems, promoters derived from the genome of plant cells (*e.g.*, heat shock promoters; the promoter for the small subunit of RUBISCO; the promoter for the chlorophyll a/b binding protein) or from plant viruses (*e.g.*, the 35S RNA promoter of CaMV; the coat protein promoter of TMV) may be used; when cloning in mammalian cell systems, promoters derived from the genorne of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used; when generating cell lines that contain multiple copies of the kinase domain

DNA, SV4O-, BPV- and EBV-based vectors may be used with an appropriate selectable marker.

[0176] Exemplary methods describing methods of DNA manipulation, vectors, various types of cells used, methods of incorporating the vectors into the cells, expression techniques, protein purification and isolation methods, and protein concentration methods are disclosed in detail in PCT publication WO 96/18738. This publication is incorporated herein by reference in its entirety, including any drawings. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

Crystal Growth

[0177] Crystals are grown from an aqueous solution containing the purified and concentrated polypeptide by a variety of techniques. These techniques include batch, liquid, bridge, dialysis, vapor diffusion, and hanging and sitting drop methods. McPherson (1982) John Wiley, New York; McPherson (1990) *Eur. J. Biochem.* 189:1-23; Webber (1991) *Adv. Protein Chem.* 41:1-36, incorporated by reference herein in their entireties, including all figures, tables, and drawings.

[0178] The native crystals of the invention are, in general, grown by adding precipitants to the concentrated solution of the polypeptide. The precipitants are added at a concentration just below that necessary to precipitate the protein. Water is removed by controlled evaporation to produce precipitating conditions, which are maintained until crystal growth ceases.

[0179] For crystals of the invention, exemplary crystallization conditions are described in the Examples. Those of ordinary skill in the art will recognize that the exemplary crystallization conditions can be varied. Such variations may be used alone or in combination. In addition, other crystallization conditions may be found, *e.g.*, by using crystallization screening plates to identify such other conditions. Those alternate conditions can then be optimized if needed to provide larger or better quality crystals.

[0180] Derivative crystals of the invention can be obtained by soaking native crystals in mother liquor containing salts of heavy metal atoms. Exemplary conditions for such soaking a native crystal utilizes a solution containing about 0.1 mM to about 5 mM

thimerosal, 4-chloromeruribenzoic acid or $KAu(CN)_2$ for about 2 hr to about 72 hr to provide derivative crystals suitable for use as isomorphous replacements in determining the X-ray crystal structure.

[0181] Co-crystals of the invention can be obtained by soaking a native crystal in mother liquor containing compound that binds the kinase, or can be obtained by co-crystallizing the kinase polypeptide in the presence of a binding compound.

[0182] In many cases, co-crystallization of kinase and binding compound can be accomplished using conditions identified for crystallizing the corresponding kinase without binding compound. It is advantageous if a plurality of different crystallization conditions have been identified for the kinase, and these can be tested to determine which condition gives the best co-crystals. It may also be benficial to optimize the conditions for co-crystallization. Alternatively, new crystallization conditions can be determined for obtaining co-crystals, *e.g.*, by screening for crystallization and then optimizing those conditions. Exemplary co-crystallization conditions are provided in the Examples.

Determining Unit Cell Dimensions and the Three Dimensional Structure of a Polypeptide or Polypeptide Complex

[0183] Once the crystal is grown, it can be placed in a glass capillary tube or other mounting device and mounted onto a holding device connected to an X-ray generator and an X-ray detection device. Collection of X-ray diffraction patterns are well documented by those in the art. See, *e.g.*, Ducruix and Geige, (1992), IRL Press, Oxford, England, and references cited therein. A beam of X-rays enters the crystal and then diffracts from the crystal. An X-ray detection device can be utilized to record the diffraction patterns emanating from the crystal. Although the X-ray detection device on older models of these instruments is a piece of film, modern instruments digitally record X-ray diffraction scattering. X-ray sources can be of various types, but advantageously, a high intensity source is used, *e.g.*, a synchrotron beam source.

[0184] Methods for obtaining the three dimensional structure of the crystalline form of a peptide molecule or molecule complex are well known in the art. See, *e.g.*, Ducruix and Geige, (1992), IRL Press, Oxford, England, and references cited therein. The following

are steps in the process of determining the three dimensional structure of a molecule or complex from X-ray diffraction data.

[0185] After the X-ray diffraction patterns are collected from the crystal, the unit cell dimensions and orientation in the crystal can be determined. They can be determined from the spacing between the diffraction emissions as well as the patterns made from these emissions. The unit cell dimensions are characterized in three dimensions in units of Angstroms (one Å= 10^{-10} meters) and by angles at each vertices. The symmetry of the unit cell in the crystals is also characterized at this stage. The symmetry of the unit cell in the crystal simplifies the complexity of the collected data by identifying repeating patterns. Application of the symmetry and dimensions of the unit cell is described below.

[0186] Each diffraction pattern emission is characterized as a vector and the data collected at this stage of the method determines the amplitude of each vector. The phases of the vectors can be determined using multiple techniques. In one method, heavy atoms can be soaked into a crystal, a method called isomorphous replacement, and the phases of the vectors can be determined by using these heavy atoms as reference points in the X-ray analysis. (Otwinowski, (1991), Daresbury, United Kingdom, 80-86). The isomorphous replacement method usually utilizes more than one heavy atom derivative.

[0187] In another method, the amplitudes and phases of vectors from a crystalline polypeptide with an already determined structure can be applied to the amplitudes of the vectors from a crystalline polypeptide of unknown structure and consequently determine the phases of these vectors. This second method is known as molecular replacement and the protein structure which is used as a reference should have a closely related structure to the protein of interest. (Naraza (1994) *Proteins* 11:281-296). Thus, the vector information from a kinase of known structure, such as those reported herein, are useful for the molecular replacement analysis of another kinase with unknown structure.

[0188] Once the phases of the vectors describing the unit cell of a crystal are determined, the vector amplitudes and phases, unit cell dimensions, and unit cell symmetry can be used as terms in a Fourier transform function. The Fourier transform function calculates the electron density in the unit cell from these measurements. The electron density that describes one of the molecules or one of the molecule complexes in the unit cell can be referred to as an electron density map. The amino acid structures of the sequence or the

molecular structures of compounds complexed with the crystalline polypeptide may then be fitted to the electron density using a variety of computer programs. This step of the process is sometimes referred to as model building and can be accomplished by using computer programs such as Turbo/FRODO or "O". (Jones (1985) *Methods in Enzymology* 115:157-171).

[0189] A theoretical electron density map can then be calculated from the amino acid structures fit to the experimentally determined electron density. The theoretical and experimental electron density maps can be compared to one another and the agreement between these two maps can be described by a parameter called an R-factor. A low value for an R-factor describes a high degree of overlapping electron density between a theoretical and experimental electron density map.

[0190] The R-factor is then minimized by using computer programs that refine the theoretical electron density map. A computer program such as X-PLOR can be used for model refinement by those skilled in the art. (Brünger (1992) *Nature* 355:472-475.) Refinement may be achieved in an iterative process. A first step can entail altering the conformation of atoms defined in an electron density map. The conformations of the atoms can be altered by simulating a rise in temperature, which will increase the vibrational frequency of the bonds and modify positions of atoms in the structure. At a particular point in the atomic perturbation process, a force field, which typically defines interactions between atoms in terms of allowed bond angles and bond lengths, Van der Waals interactions, hydrogen bonds, ionic interactions, and hydrophobic interactions, can be applied to the system of atoms. Favorable interactions may be described in terms of free energy and the atoms can be moved over many iterations until a free energy minimum is achieved. The refinement process can be iterated until the R-factor reaches a minimum value.

[0191] The three dimensional structure of the molecule or molecule complex is described by atoms that fit the theoretical electron density characterized by a minimum R-value. A file can then be created for the three dimensional structure that defines each atom by coordinates in three dimensions. An example of such a structural coordinate file is shown in Table 1.

IV. Structures of PYK2

[0192] The present invention provides high-resolution three-dimensional structures and atomic structure coordinates of crystalline PYK2 kinase domain and PYK2 kinase domain co-complexed with exemplary binding compounds as determined by X-ray crystallography. The methods used to obtain the structure coordinates are provided in the examples. The atomic structure coordinates of crystalline PYK2 are listed in Table 1, and atomic coordinates for PYK2 co-crystallized with AMPPNP are provided in Table 2. Co-crystal coordinates can be used in the same way, *e.g.*, in the various aspects described herein, as coordinates for the protein by itself.

[0193] Those having skill in the art will recognize that atomic structure coordinates as determined by X-ray crystallography are not without error. Thus, it is to be understood that any set of structure coordinates obtained for crystals of PYK2, whether native crystals, kinase domain crystals, derivative crystals or co-crystals, that have a root mean square deviation ("r.m.s.d.") of less than or equal to about 1.5 Å when superimposed, using backbone atoms (N, C_α, C and 0), on the structure coordinates listed in Table 1 (or Table 2) are considered to be identical with the structure coordinates listed in the Table 1 (or Table 2) when at least about 50% to 100% of the backbone atoms of PYK2 or PYK2 kinase domain are included in the superposition.

V. Uses of the Crystals and Atomic Structure Coordinates

[0194] The crystals of the invention, and particularly the atomic structure coordinates obtained therefrom, have a wide variety of uses. For example, the crystals described herein can be used as a starting point in any of the methods of use for kinases known in the art or later developed. Such methods of use include, for example, identifying molecules that bind to the native or mutated catalytic domain of kinases. The crystals and structure coordinates are particularly useful for identifying ligands that modulate kinase activity as an approach towards developing new therapeutic agents. In particular, the crystals and structural information are useful in methods for ligand development utilizing molecular scaffolds.

[0195] The structure coordinates described herein can be used as phasing models or homology models for determining the crystal structures of additional kinases, as well as the structures of co-crystals of such kinases with ligands such as inhibitors, agonists, antagonists, and other molecules. The structure coordinates, as well as models of the three-

dimensional structures obtained therefrom, can also be used to aid the elucidation of solution-based structures of native or mutated kinases, such as those obtained via NMR.

VI. Electronic Representations of Kinase Structures

[0196] Structural information of kinases or portions of kinases (*e.g.*, kinase active sites) can be represented in many different ways. Particularly useful are electronic representations, as such representations allow rapid and convenient data manipulations and structural modifications. Electronic representations can be embedded in manydifferent storage or memory media, frequently computer readable media. Examples include without limitations, computer random access memory (RAM), floppy disk, magnetic hard drive, magnetic tape (analog or digital), compact disk (CD), optical disk, CD-ROM, memory card, digital video disk (DVD), and others. The storage medium can be separate or part of a computer system. Such a computer system may be a dedicated, special purpose, or embedded system, such as a computer system that forms part of an X-ray crystallography system, or may be a general purpose computer (which may have data connection with other equipment such as a sensor device in an X-ray crystallographic system. In many cases, the information provided by such electronic representations can also be represented physically or visually in two or three dimensions, *e.g.*, on paper, as a visual display (*e.g.*, on a computer monitor as a two-dimensional or pseudo-three-dimensional image) or as a three-dimensional physical model. Such physical representations can also be used, alone or in connection with electronic representations. Exemplary useful representations include, but are not limited to, the following:

Atomic Coordinate Representation

[0197] One type of representation is a list or table of atomic coordinates representing positions of particular atoms in a molecular structure, portions of a structure, or complex (*e.g.*, a co-crystal). Such a representation may also include additional information, for example, information about occupancy of particular coordinates. One such atomic coordinate representation contains the coordinate information of Table 1 in electronic form.

Energy Surface or Surface of Interaction Representation

[0198] Another representation is an energy surface representation, *e.g.*, of an active site or other binding site, representing an energy surface for electronic and steric interactions. Such a representation may also include other features. An example is the inclusion of representation of a particular amino acid residue(s) or group(s) on a particular amino acid residue(s), *e.g.*, a residue or group that can participate in H-bonding or ionic interaction. Such energy surface representations can be readily generated from atomic coordinate representations using any of a variety of available computer programs.

Structural Representation

[0199] Still another representation is a structural representation, *i.e.*, a physical representation or an electronic representation of such a physical representation. Such a structural representation includes representations of relative positions of particular features of a molecule or complex, often with linkage between structural features. For example, a structure can be represented in which all atoms are linked; atoms other than hydrogen are linked; backbone atoms, with or without representation of sidechain atoms that could participate in significant electronic interaction, are linked; among others. However, not all features need to be linked. For example, for structural representations of portions of a molecule or complex, structural features significant for that feature may be represented (*e.g.*, atoms of amino acid residues that can have significant binding interation with a ligand at a binding site. Those amino acid residues may not be linked with each other.

[0200] A structural representation can also be a schematic representation. For example, a schematic representation can represent secondary and/or tertiary structure in a schematic manner. Within such a schematic representation of a polypeptide, a particular amino acid residue(s) or group(s) on a residue(s) can be included, *e.g.*, conserved residues in a binding site, and/or residue(s) or group(s) that may interact with binding compounds. Electronic structural representations can be generated, for example, from atomic coordinate information using computer programs designed for that function and/or by constructing an electronic representation with manual input based on interpretation of another form of structural information. Physical representations can be created, for example, by printing an image of a computer-generated image, by constructing a 3D model.

VII. Structure Determination for Kinases with Unknown Structure Using Structural Coordinates

[0201] Structural coordinates, such as those set forth in Table 1, can be used to determine the three dimensional structures of kinases with unknown structure. The methods described below can apply structural coordinates of a polypeptide with known structure to another data set, such as an amino acid sequence, X-ray crystallographic diffraction data, or nuclear magnetic resonance (NMR) data. Preferred embodiments of the invention relate to determining the three dimensional structures of other serine/threonine kinases, and related polypeptides.

Structures Using Amino Acid Homology

[0202] Homology modeling is a method of applying structural coordinates of a polypeptide of known structure to the amino acid sequence of a polypeptide of unknown structure. This method is accomplished using a computer representation of the three dimensional structure of a polypeptide or polypeptide complex, the computer representation of amino acid sequences of the polypeptides with known and unknown structures, and standard computer representations of the structures of amino acids. Homology modeling generally involves (a) aligning the amino acid sequences of the polypeptides with and without known structure; (b) transferring the coordinates of the conserved amino acids in the known structure to the corresponding amino acids of the polypeptide of unknown structure; refining the subsequent three dimensional structure; and (d) constructing structures of the rest of the polypeptide. One skilled in the art recognizes that conserved amino acids between two proteins can be determined from the sequence alignment step in step (a).

[0203] The above method is well known to those skilled in the art. (Greer (1985) *Science* 228:1055; Blundell et *al.* A(1988) *Eur. J. Biochem.* 172:513. An exemplary computer program that can be utilized for homology modeling by those skilled in the art is the Homology module in the Insight II modeling package distributed by Accelerys Inc.

[0204] Alignment of the amino acid sequence is accomplished by first placing the computer representation of the amino acid sequence of a polypeptide with known structure above the amino acid sequence of the polypeptide of unknown structure. Amino acids in the sequences are then compared and groups of amino acids that are homologous (e.g., amino acid side chains that are similar in chemical nature - aliphatic, aromatic, polar, or charged) are grouped together. This method will detect conserved regions of the

polypeptides and account for amino acid insertions or deletions. Such alignment and/or can also be performed fully electronically using sequence alignment and analyses software.

[0205] Once the amino acid sequences of the polypeptides with known and unknown structures are aligned, the structures of the conserved amino acids in the computer representation of the polypeptide with known structure are transferred to the corresponding amino acids of the polypeptide whose structure is unknown. For example, a tyrosine in the amino acid sequence of known structure may be replaced by a phenylalanine, the corresponding homologous amino acid in the amino acid sequence of unknown structure.

[0206] The structures of amino acids located in non-conserved regions are to be assigned manually by either using standard peptide geometries or molecular simulation techniques, such as molecular dynamics. The final step in the process is accomplished by refining the entire structure using molecular dynamics and/or energy minimization. The homology modeling method is well known to those skilled in the art and has been practiced using different protein molecules. For example, the three dimensional structure of the polypeptide corresponding to the catalytic domain of a serine/threonine protein kinase, myosin light chain protein kinase, was homology modeled from the cAMP-dependent protein kinase catalytic subunit. (Knighton et *al.* (1992) *Science* 258:130-135.)

Structures Using Molecular Replacement

[0207] Molecular replacement is a method of applying the X-ray diffraction data of a polypeptide of known structure to the X-ray diffraction data of a polypeptide of unknown sequence. This method can be utilized to define the phases describing the X-ray diffraction data of a polypeptide of unknown structure when only the amplitudes are known. X-PLOR is a commonly utilized computer software package used for molecular replacement. Brünger (1992) *Nature* 355:472-475. AMORE is another program used for molecular replacement. Navaza (1994) *Acta Crystallogr.* A50:157-163. Preferably, the resulting structure does not exhibit a root-mean-square deviation of more than 3Å.

[0208] A goal of molecular replacement is to align the positions of atoms in the unit cell by matching electron diffraction data from two crystals. A program such as X-PLOR can involve four steps. A first step can be to determine the number of molecules in the unit cell

and define the angles between them. A second step can involve rotating the diffraction data to define the orientation of the molecules in the unit cell. A third step can be to translate the electron density in three dimensions to correctly position the molecules in the unit cell. Once the amplitudes and phases of the X-ray diffraction data is determined, an R-factor can be calculated by comparing electron diffraction maps calculated experimentally from the reference data set and calculated from the new data set. An R-factor between 30-50% indicates that the orientations of the atoms in the unit cell are reasonably determined by this method. A fourth step in the process can be to decrease the R-factor to roughly 20% by refining the new electron density map using iterative refinement techniques described herein and known to those or ordinary skill in the art.

Structures Using NMR Data

[0209] Structural coordinates of a polypeptide or polypeptide complex derived from X-ray crystallographic techniques can be applied towards the elucidation of three dimensional structures of polypeptides from nuclear magnetic resonance (NMR) data. This method is used by those skilled in the art. (Wuthrich, (1986), John Wiley and Sons, New York:176-199; Pflugrath et *al.* (1986) *J. Mol. Biol.* 189:383-386; Kline *et al.* (1986) *J. Mol. Biol.* 189:377-382.) While the secondary structure of a polypeptide is often readily determined by utilizing two-dimensional NMR data, the spatial connections between individual pieces of secondary structure are not as readily determinable. The coordinates defining a three-dimensional structure of a polypeptide derived from X-ray crystallographic techniques can guide the NMR spectroscopist to an understanding of these spatial interactions between secondary structural elements in a polypeptide of related structure.

[0210] The knowledge of spatial interactions between secondary structural elements can greatly simplify Nuclear Overhauser Effect (NOE) data from two-dimensional NMR experiments. Additionally, applying the crystallographic coordinates after the determination of secondary structure by NMR techniques only simplifies the assignment of NOEs relating to particular amino acids in the polypeptide sequence and does not greatly bias the NMR analysis of polypeptide structure. Conversely, using the crystallographic coordinates to simplify NOE data while determining secondary structure of the polypeptide would bias the NMR analysis of protein structure.

VIII. Structure-Based Design of Modulators of Kinase Function Utilizing Structural Coordinates

[0211] Structure-based modulator design and identification methods are powerful techniques that can involve searches of computer databases containing a wide variety of potential modulators and chemical functional groups. The computerized design and identification of modulators is useful as the computer databases contain more compounds than the chemical libraries, often by an order of magnitude. For reviews of structure-based drug design and identification (*see* Kuntz et *al.* (1994), *Acc. Chem. Res.* 27:117; Guida (1994) *Current Opinion in Struc. Biol.* 4: 777; Colman (1994) *Current Opinion in Struc. Biol.* 4: 868).

[0212] The three dimensional structure of a polypeptide defined by structural coordinates can be utilized by these design methods, for example, the structural coordinates of Table 1. In addition, the three dimensional structures of kinases determined by the homology, molecular replacement, and NMR techniques described herein can also be applied to modulator design and identification methods.

[0213] For identifying modulators, structural information for a native kinase, in particular, structural information for the active site of the kinase, can be used. However, it may be advantageous to utilize structural information from one or more co-crystals of the kinase with one or more binding compounds. It can also be advantageous if the binding compound has a structural core in common with test compounds.

Design by Searching Molecular Data Bases

[0214] One method of rational design searches for modulators by docking the computer representations of compounds from a database of molecules. Publicly available databases include, for example:

a) ACD from Molecular Designs Limited
b) NCI from National Cancer Institute
c) CCDC from Cambridge Crystallographic Data Center
d) CAST from Chemical Abstract Service
e) Derwent from Derwent Information Limited
f) Maybridge from Maybridge Chemical Company LTD
g) Aldrich from Aldrich Chemical Company

h) Directory of Natural Products from Chapman & Hall

[0215] One such data base (ACD distributed by Molecular Designs Limited Information Systems) contains compounds that are synthetically derived or are natural products. Methods available to those skilled in the art can convert a data set represented in two dimensions to one represented in three dimensions. These methods are enabled by such computer programs as CONCORD from Tripos Associates or DE-Converter from Molecular Simulations Limited.

[0216] Multiple methods of structure-based modulator design are known to those in the art. (Kuntz et *al.,* (1982), *J. Mol. Biol. 162:* 269; Kuntz et aZ., (1994), Acc. *Chern. Res. 27:* 117; Meng *et al.,* (1992), *J. Compt. Chem. 13:* 505; Bohm, (1994), *J. Comp. Aided Molec. Design 8:* 623.)

[0217] A computer program widely utilized by those skilled in the art of rational modulator design is DOCK from the University of California in San Francisco. The general methods utilized by this computer program and programs like it are described in three applications below. More detailed information regarding some of these techniques can be found in the Accelerys User Guide, 1995. A typical computer program used for this purpose can perform a processes comprising the following steps or functions:

(a) remove the existing compound from the protein;

(b) dock the structure of another compound into the active-site using the computer program (such as DOCK) or by interactively moving the compound into the active-site;

(c) characterize the space between the compound and the active-site atoms;

(d) search libraries for molecular fragments which (i) can fit into the empty space between the compound and the active-site, and (ii) can be linked to the compound; and

(e) link the fragments found above to the compound and evaluate the new modified compound.

[0218] Part (c) refers to characterizing the geometry and the complementary interactions formed between the atoms of the active site and the compounds. A favorable geometric fit is attained when a significant surface area is shared between the compound and active-site atoms without forming unfavorable steric interactions.One skilled in the art would note

that the method can be performed by skipping parts (d) and (e) and screening a database of many compounds.

[0219] Structure-based design and identification of modulators of kinase function can be used in conjunction with assay screening. As large computer databases of compounds (around 10,000 compounds) can be searched in a matter of hours or even less, the computer-based method can narrow the compounds tested as potential modulators of kinase function in biochemical or cellular assays.

[0220] The above descriptions of structure-based modulator design are not all encompassing and other methods are reported in the literature and can be used, *e.g.*:

(1) CAVEAT: Bartlett *et* al.,(1989), in Chemical and Biological Problems in Molecular Recognition, Roberts, S.M.; Ley, S.V.; Campbell, M.M. eds.; *Royal Society of Chemistry*: Cambridge, pp.182-196.

(2) FLOG: Miller et al., (1994), *J. Comp. Aided Molec. Design* 8:153.

(3) PRO Modulator: Clark *et al.*, (1995), *J. Comp. Aided Molec. Design* 9:13.

(4) MCSS: Miranker and Karplus, (1991), *Proteins: Structure, Function, and Genetics 11:29.*

(5) AUTODOCK: Goodsell and Olson, (1990), *Proteins: Structure, Function, and Genetics 8:195.*

(6) GRID: Goodford, (1985), *J. Med. Chem.* 28:849.

Design by Modifying Compounds in Complex with PYK2 Kinase

[0221] Another way of identifying compounds as potential modulators is to modify an existing modulator in the polypeptide active site. For example, the computer representation of modulators can be modified within the computer representation of a PYK2 active site. Detailed instructions for this technique can be found, for example, in the Accelerys User Manual, 1995 in LUDI. The computer representation of the modulator is typically modified by the deletion of a chemical group or groups or by the addition of a chemical group or groups.

[0222] Upon each modification to the compound, the atoms of the modified compound and active site can be shifted in conformation and the distance between the modulator and the active-site atoms may be scored along with any complementary interactions formed between the two molecules. Scoring can be complete when a favorable geometric fit and

favorable complementary interactions are attained. Compounds that have favorable scores are potential modulators.

Design by Modifying the Structure of Compounds that Bind PYK2 Kinase

[0223] A third method of structure-based modulator design is to screen compounds designed by a modulator building or modulator searching computer program. Examples of these types of programs can be found in the Molecular Simulations Package, Catalyst. Descriptions for using this program are documented in the Molecular Simulations User Guide (1995). Other computer programs used in this application are ISIS/HOST, ISIS/BASE, ISIS/DRAW) from Molecular Designs Limited and UNITY from Tripos Associates.

[0224] These programs can be operated on the structure of a compound that has been removed from the active site of the three dimensional structure of a compound-kinase complex. Operating the program on such a compound is preferable since it is in a biologically active conformation.

[0225] A modulator construction computer program is a computer program that may be used to replace computer representations of chemical groups in a compound complexed with a kinase or other biomolecule with groups from a computer database. A modulator searching computer program is a computer program that may be used to search computer representations of compounds from a computer data base that have similar three dimensional structures and similar chemical groups as compound bound to a particular biomolecule.

[0226] A typical program can operate by using the following general steps:

(a) map the compounds by chemical features such as by hydrogen bond donors or acceptors, hydrophobic/lipophilic sites, positively ionizable sites, or negatively ionizable sites;

(b) add geometric constraints to the mapped features; and

(c) search databases with the model generated in (b).

[0227] Those skilled in the art also recognize that not all of the possible chemical features of the compound need be present in the model of (b). One can use any subset of the model to generate different models for data base searches.

Modulator Design Using Molecular Scaffolds

[0228] The present invention can also advantageously utilize methods for designing compounds, designated as molecular scaffolds, that can act broadly across families of molecules and/or for using a molecular scaffold to design ligands that target individual or multiple members of those families. In preferred embodiments, the molecules can be proteins and a set of chemical compounds can be assembled that have properties such that they are 1) chemically designed to act on certain protein families and/or 2) behave more like molecular scaffolds, meaning that they have chemical substructures that make them specific for binding to one or more proteins in a family of interest. Alternatively, molecular scaffolds can be designed that are preferentially active on an individual target molecule.

[0229] Useful chemical properties of molecular scaffolds can include one or more of the following characteristics, but are not limited thereto: an average molecular weight below about 350 daltons, or between from about 150 to about 350 daltons, or from about 150 to about 300 daltons; having a clogP below 3; a number of rotatable bonds of less than 4; a number of hydrogen bond donors and acceptors below 5 or below 4; a polar surface area of less than 50 $Å^2$; binding at protein binding sites in an orientation so that chemical substituents from a combinatorial library that are attached to the scaffold can be projected into pockets in the protein binding site; and possessing chemically tractable structures at its substituent attachment points that can be modified, thereby enabling rapid library construction.

[0230] By "clog P" is meant the calculated log P of a compound, "P" referring to the partition coefficient between octanol and water.

[0231] The term "Molecular Polar Surface Area (PSA)" refers to the sum of surface contributions of polar atoms (usually oxygens, nitrogens and attached hydrogens) in a molecule. The polar surface area has been shown to correlate well with drug transport properties, such as intestinal absorption, or blood-brain barrier penetration.

[0232] Additional useful chemical properties of distinct compounds for inclusion in a combinatorial library include the ability to attach chemical moieties to the compound that will not interfere with binding of the compound to at least one protein of interest, and that will impart desirable properties to the library members, for example, causing the library

members to be actively transported to cells and/or organs of interest, or the ability to attach to a device such as a chromatography column (*e.g.*, a streptavidin column through a molecule such as biotin) for uses such as tissue and proteomics profiling purposes.

[0233] A person of ordinary skill in the art will realize other properties that can be desirable for the scaffold or library members to have depending on the particular requirements of the use, and that compounds with these properties can also be sought and identified in like manner. Methods of selecting compounds for assay are known to those of ordinary skill in the art, for example, methods and compounds described in U.S. Patent No. 6,288,234, 6,090,912, 5,840,485, each of which is hereby incorporated by reference in its entirety, including all charts and drawings.

[0234] In various embodiments, the present invention provides methods of designing ligands that bind to a plurality of members of a molecular family, where the ligands contain a common molecular scaffold. Thus, a compound set can be assayed for binding to a plurality of members of a molecular family, *e.g.*, a protein family. One or more compounds that bind to a plurality of family members can be identified as molecular scaffolds. When the orientation of the scaffold at the binding site of the target molecules has been determined and chemically tractable structures have been identified, a set of ligands can be synthesized starting with one or a few molecular scaffolds to arrive at a plurality of ligands, wherein each ligand binds to a separate target molecule of the molecular family with altered or changed binding affinity or binding specificity relative to the scaffold. Thus, a plurality of drug lead molecules can be designed to preferentially target individual members of a molecular family based on the same molecular scaffold, and act on them in a specific manner.

IX. Binding Assays

[0235] The methods of the present invention can involve assays that are able to detect the binding of compounds to a target molecule. Such binding is at a statistically significant level, preferably with a confidence level of at least 90%, more preferably at least 95, 97, 98, 99% or greater confidence level that the assay signal represents binding to the target molecule, *i.e.*, is distinguished from background. Preferably controls are used to distinguish target binding from non-specific binding. The assays of the present invention can also include assaying compounds for low affinity binding to the target molecule. A

large variety of assays indicative of binding are known for different target types and can be used for this invention. Compounds that act broadly across protein families are not likely to have a high affinity against individual targets, due to the broad nature of their binding. Thus, assays described herein allow for the identification of compounds that bind with low affinity, very low affinity, and extremely low affinity. Therefore, potency (or binding affinity) is not the primary, nor even the most important, indicia of identification of a potentially useful binding compound. Rather, even those compounds that bind with low affinity, very low affinity, or extremely low affinity can be considered as molecular scaffolds that can continue to the next phase of the ligand design process.

[0236] By binding with "low affinity" is meant binding to the target molecule with a dissociation constant (k_d) of greater than 1 μM under standard conditions. By binding with "very low affinity" is meant binding with a k_d of above about 100 μM under standard conditions. By binding with "extremely low affinity" is meant binding at a k_d of above about 1 mM under standard conditions. By "moderate affinity" is meant binding with a k_d of from about 200 nM to about 1 μM under standard conditions. By "moderately high affinity" is meant binding at a k_d of from about 1 nM to about 200 nM. By binding at "high affinity" is meant binding at a k_d of below about 1 nM under standard conditions. For example, low affinity binding can occur because of a poorer fit into the binding site of the target molecule or because of a smaller number of non-covalent bonds, or weaker covalent bonds present to cause binding of the scaffold or ligand to the binding site of the target molecule relative to instances where higher affinity binding occurs. The standard conditions for binding are at pH 7.2 at 37°C for one hour. For example, 100 μl/well can be used in HEPES 50 mM buffer at pH 7.2, NaCl 15 mM, ATP 2 μM, and bovine serum albumin 1 ug/well, 37°C for one hour.

[0237] Binding compounds can also be characterized by their effect on the activity of the target molecule. Thus, a "low activity" compound has an inhibitory concentration (IC_{50}) or excitation concentration (EC_{50}) of greater than 1 μM under standard conditions. By "very low activity" is meant an IC_{50} or EC_{50} of above 100 μM under standard conditions. By "extremely low activity" is meant an IC_{50} or EC_{50} of above 1 mM under standard conditions. By "moderate activity" is meant an IC_{50} or EC_{50} of 200 nM to 1 μM under standard conditions. By "moderately high activity" is meant an IC_{50} or EC_{50} of 1 nM to 200 nM. By "high activity" is meant an IC_{50} or EC_{50} of below 1 nM under standard

conditions. The IC_{50} (or EC_{50}) is defined as the concentration of compound at which 50% of the activity of the target molecule (e.g., enzyme or other protein) activity being measured is lost (or gained) relative to activity when no compound is present. Activity can be measured using methods known to those of ordinary skill in the art, *e.g.*, by measuring any detectable product or signal produced by occurrence of an enzymatic reaction, or other activity by a protein being measured.

[0238] By "background signal" in reference to a binding assay is meant the signal that is recorded under standard conditions for the particular assay in the absence of a test compound, molecular scaffold, or ligand that binds to the target molecule. Persons of ordinary skill in the art will realize that accepted methods exist and are widely available for determining background signal.

[0239] By "standard deviation" is meant the square root of the variance. The variance is a measure of how spread out a distribution is. It is computed as the average squared deviation of each number from its mean. For example, for the numbers 1, 2, and 3, the mean is 2 and the variance is:

$$\sigma^2 = \frac{(1-2)^2 + (2-2)^2 + (3-2)^2}{3} = 0.667$$

[0240] To design or discover scaffolds that act broadly across protein families, proteins of interest can be assayed against a compound collection or set. The assays can preferably be enzymatic or binding assays. In some embodiments it may be desirable to enhance the solubility of the compounds being screened and then analyze all compounds that show activity in the assay, including those that bind with low affinity or produce a signal with greater than about three times the standard deviation of the background signal. The assays can be any suitable assay such as, for example, binding assays that measure the binding affinity between two binding partners. Various types of screening assays that can be useful in the practice of the present invention are known in the art, such as those described in U.S. Patent Nos. 5,763,198, 5,747,276, 5,877,007, 6,243,980, 6,294,330, and 6,294,330, each of which is hereby incorporated by reference in its entirety, including all charts and drawings.

[0241] In various embodiments of the assays at least one compound, at least about 5%, at least about 10%, at least about 15%, at least about 20%, or at least about 25% of the compounds can bind with low affinity. In general, up to about 20% of the compounds can show activity in the screening assay and these compounds can then be analyzed directly with high-throughput co-crystallography, computational analysis to group the compounds into classes with common structural properties (e.g., structural core and/or shape and polarity characteristics), and the identification of common chemical structures between compounds that show activity.

[0242] The person of ordinary skill in the art will realize that decisions can be based on criteria that are appropriate for the needs of the particular situation, and that the decisions can be made by computer software programs. Classes can be created containing almost any number of scaffolds, and the criteria selected can be based on increasingly exacting criteria until an arbitrary number of scaffolds is arrived at for each class that is deemed to be advantageous.

Surface Plasmon Resonance

[0243] Binding parameters can be measured using surface plasmon resonance, for example, with a BIAcore® chip (Biacore, Japan) coated with immobilized binding components. Surface plasmon resonance is used to characterize the microscopic association and dissociation constants of reaction between an sFv or other ligand directed against target molecules. Such methods are generally described in the following references which are incorporated herein by reference. Vely F. et al., (2000) BIAcore® analysis to test phosphopeptide-SH2 domain interactions, *Methods in Molecular Biology.* 121:313-21; Liparoto et al., (1999) Biosensor analysis of the interleukin-2 receptor complex, *Journal of Molecular Recognition.* 12:316-21; Lipschultz et al., (2000) Experimental design for analysis of complex kinetics using surface plasmon resonance, *Methods.* 20(3):310-8; Malmqvist., (1999) BIACORE: an affinity biosensor system for characterization of biomolecular interactions, Biochemical Society Transactions 27:335-40; Alfthan, (1998) Surface plasmon resonance biosensors as a tool in antibody engineering, *Biosensors & Bioelectronics.* 13:653-63; Fivash et al., (1998) BIAcore for macromolecular interaction, Current Opinion in Biotechnology. 9:97-101; Price et al.; (1998) Summary report on the ISOBM TD-4 Workshop: analysis of 56 monoclonal antibodies against the MUC1 mucin. *Tumour Biology* 19 Suppl 1:1-20; Malmqvist et al,

(1997) Biomolecular interaction analysis: affinity biosensor technologies for functional analysis of proteins, *Current Opinion in Chemical Biology*. 1:378-83; O'Shannessy et al., (1996) Interpretation of deviations from pseudo-first-order kinetic behavior in the characterization of ligand binding by biosensor technology, *Analytical Biochemistry*. 236:275-83; Malmborg et al., (1995) BIAcore as a tool in antibody engineering, *Journal of Immunological Methods*. 183:7-13; Van Regenmortel, (1994) Use of biosensors to characterize recombinant proteins, *Developments in Biological Standardization*. 83:143-51; and O'Shannessy, (1994) Determination of kinetic rate and equilibrium binding constants for macromolecular interactions: a critique of the surface plasmon resonance literature, *Current Opinions in Biotechnology*. 5:65-71.

[0244] BIAcore® uses the optical properties of surface plasmon resonance (SPR) to detect alterations in protein concentration bound to a dextran matrix lying on the surface of a gold/glass sensor chip interface, a dextran biosensor matrix. In brief, proteins are covalently bound to the dextran matrix at a known concentration and a ligand for the protein is injected through the dextran matrix. Near infrared light, directed onto the opposite side of the sensor chip surface is reflected and also induces an evanescent wave in the gold film, which in turn, causes an intensity dip in the reflected light at a particular angle known as the resonance angle. If the refractive index of the sensor chip surface is altered (e.g., by ligand binding to the bound protein) a shift occurs in the resonance angle. This angle shift can be measured and is expressed as resonance units (RUs) such that 1000 RUs is equivalent to a change in surface protein concentration of 1 ng/mm^2. These changes are displayed with respect to time along the y-axis of a sensorgram, which depicts the association and dissociation of any biological reaction.

High Throughput Screening (HTS) Assays

[0245] HTS typically uses automated assays to search through large numbers of compounds for a desired activity. Typically HTS assays are used to find new drugs by screening for chemicals that act on a particular enzyme or molecule. For example, if a chemical inactivates an enzyme it might prove to be effective in preventing a process in a cell which causes a disease. High throughput methods enable researchers to assay thousands of different chemicals against each target molecule very quickly using robotic handling systems and automated analysis of results.

[0246] As used herein, "high throughput screening" or "HTS" refers to the rapid in vitro screening of large numbers of compounds (libraries); generally tens to hundreds of thousands of compounds, using robotic screening assays. Ultra high-throughput Screening (uHTS) generally refers to the high-throughput screening accelerated to greater than 100,000 tests per day.

[0247] To achieve high-throughput screening, it is advantageous to house samples on a multicontainer carrier or platform. A multicontainer carrier facilitates measuring reactions of a plurality of candidate compounds simultaneously. Multi-well microplates may be used as the carrier. Such multi-well microplates, and methods for their use in numerous assays, are both known in the art and commercially available.

[0248] Screening assays may include controls for purposes of calibration and confirmation of proper manipulation of the components of the assay. Blank wells that contain all of the reactants but no member of the chemical library are usually included. As another example, a known inhibitor (or activator) of an enzyme for which modulators are sought, can be incubated with one sample of the assay, and the resulting decrease (or increase) in the enzyme activity used as a comparator or control. It will be appreciated that modulators can also be combined with the enzyme activators or inhibitors to find modulators which inhibit the enzyme activation or repression that is otherwise caused by the presence of the known the enzyme modulator. Similarly, when ligands to a sphingolipid target are sought, known ligands of the target can be present in control/calibration assay wells.

Measuring Enzymatic and Binding Reactions During Screening Assays

[0249] Techniques for measuring the progression of enzymatic and binding reactions, e.g., in multicontainer carriers, are known in the art and include, but are not limited to, the following.

[0250] Spectrophotometric and spectrofluorometric assays are well known in the art. Examples of such assays include the use of colorimetric assays for the detection of peroxides, as disclosed in Example 1(b) and Gordon, A. J. and Ford, R. A., (1972) The Chemist's Companion: A Handbook Of Practical Data, Techniques, And References, John Wiley and Sons, N.Y., Page 437.

[0251] Fluorescence spectrometry may be used to monitor the generation of reaction products. Fluorescence methodology is generally more sensitive than the absorption methodology. The use of fluorescent probes is well known to those skilled in the art. For reviews, see Bashford et al., (1987) Spectrophotometry and Spectrofluorometry: A Practical Approach, pp. 91-114, IRL Press Ltd.; and Bell, (1981) Spectroscopy In Biochemistry, Vol. I, pp. 155-194, CRC Press.

[0252] In spectrofluorometric methods, enzymes are exposed to substrates that change their intrinsic fluorescence when processed by the target enzyme. Typically, the substrate is nonfluorescent and is converted to a fluorophore through one or more reactions. As a non-limiting example, SMase activity can be detected using the Amplex® Red reagent (Molecular Probes, Eugene, OR). In order to measure sphingomyelinase activity using Amplex® Red, the following reactions occur. First, SMase hydrolyzes sphingomyelin to yield ceramide and phosphorylcholine. Second, alkaline phosphatase hydrolyzes phosphorylcholine to yield choline. Third, choline is oxidized by choline oxidase to betaine. Finally, H_2O_2, in the presence of horseradish peroxidase, reacts with Amplex® Red to produce the fluorescent product, Resorufin, and the signal therefrom is detected using spectrofluorometry.

[0253] Fluorescence polarization (FP) is based on a decrease in the speed of molecular rotation of a fluorophore that occurs upon binding to a larger molecule, such as a receptor protein, allowing for polarized fluorescent emission by the bound ligand. FP is empirically determined by measuring the vertical and horizontal components of fluorophore emission following excitation with plane polarized light. Polarized emission is increased when the molecular rotation of a fluorophore is reduced. A fluorophore produces a larger polarized signal when it is bound to a larger molecule (i.e. a receptor), slowing molecular rotation of the fluorophore. The magnitude of the polarized signal relates quantitatively to the extent of fluorescent ligand binding. Accordingly, polarization of the "bound" signal depends on maintenance of high affinity binding.

[0254] FP is a homogeneous technology and reactions are very rapid, taking seconds to minutes to reach equilibrium. The reagents are stable, and large batches may be prepared, resulting in high reproducibility. Because of these properties, FP has proven to be highly automatable, often performed with a single incubation with a single, premixed, tracer-

receptor reagent. For a review, see Owickiet al., (1997), Application of Fluorescence Polarization Assays in High-Throughput Screening, *Genetic Engineering News*, 17:27.

[0255] FP is particularly desirable since its readout is independent of the emission intensity (Checovich, W. J., et al., (1995) *Nature* 375:254-256; Dandliker, W. B., et al., (1981) *Methods in Enzymology* 74:3-28) and is thus insensitive to the presence of colored compounds that quench fluorescence emission. FP and FRET (see below) are well-suited for identifying compounds that block interactions between sphingolipid receptors and their ligands. See, for example, Parker et al., (2000) Development of high throughput screening assays using fluorescence polarization: nuclear receptor-ligand-binding and kinase/phosphatase assays, J Biomol Screen 5:77-88.

[0256] Fluorophores derived from sphingolipids that may be used in FP assays are commercially available. For example, Molecular Probes (Eugene, OR) currently sells sphingomyelin and one ceramide flurophores. These are, respectively, N-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene- 3-pentanoyl)sphingosyl phosphocholine (BODIPY® FL C5-sphingomyelin); N-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene- 3-dodecanoyl)sphingosyl phosphocholine (BODIPY® FL C12-sphingomyelin); and N-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene- 3-pentanoyl)sphingosine (BODIPY® FL C5-ceramide). U.S. Patent No. 4,150,949, (Immunoassay for gentamicin), discloses fluorescein-labelled gentamicins, including fluoresceinthiocarbanyl gentamicin. Additional fluorophores may be prepared using methods well known to the skilled artisan.

[0257] Exemplary normal-and-polarized fluorescence readers include the POLARION® fluorescence polarization system (Tecan AG, Hombrechtikon, Switzerland). General multiwell plate readers for other assays are available, such as the VERSAMAX® reader and the SPECTRAMAX® multiwell plate spectrophotometer (both from Molecular Devices).

[0258] Fluorescence resonance energy transfer (FRET) is another useful assay for detecting interaction and has been described. See, e.g., Heim et al., (1996) *Curr. Biol.* 6:178-182; Mitra et al., (1996) *Gene* 173:13-17; and Selvin et al., (1995) *Meth. Enzymol.* 246:300-345. FRET detects the transfer of energy between two fluorescent substances in close proximity, having known excitation and emission wavelengths. As an example, a protein can be expressed as a fusion protein with green fluorescent protein (GFP). When

two fluorescent proteins are in proximity, such as when a protein specifically interacts with a target molecule, the resonance energy can be transferred from one excited molecule to the other. As a result, the emission spectrum of the sample shifts, which can be measured by a fluorometer, such as a fMAX multiwell fluorometer (Molecular Devices, Sunnyvale Calif.).

[0259] Scintillation proximity assay (SPA) is a particularly useful assay for detecting an interaction with the target molecule. SPA is widely used in the pharmaceutical industry and has been described (Hanselman et al., (1997) *J. Lipid Res.* 38:2365-2373; Kahl et al., (1996) *Anal. Biochem.* 243:282-283; Undenfriend et al., (1987) *Anal. Biochem.* 161:494-500). See also U.S. Patent Nos. 4,626,513 and 4,568,649, and European Patent No. 0,154,734. One commercially available system uses FLASHPLATE® scintillant-coated plates (NEN Life Science Products, Boston, MA).

[0260] The target molecule can be bound to the scintillator plates by a variety of well known means. Scintillant plates are available that are derivatized to bind to fusion proteins such as GST, His6 or Flag fusion proteins. Where the target molecule is a protein complex or a multimer, one protein or subunit can be attached to the plate first, then the other components of the complex added later under binding conditions, resulting in a bound complex.

[0261] In a typical SPA assay, the gene products in the expression pool will have been radiolabeled and added to the wells, and allowed to interact with the solid phase, which is the immobilized target molecule and scintillant coating in the wells. The assay can be measured immediately or allowed to reach equilibrium. Either way, when a radiolabel becomes sufficiently close to the scintillant coating, it produces a signal detectable by a device such as a TOPCOUNT NXT® microplate scintillation counter (Packard BioScience Co., Meriden Conn.). If a radiolabeled expression product binds to the target molecule, the radiolabel remains in proximity to the scintillant long enough to produce a detectable signal.

[0262] In contrast, the labeled proteins that do not bind to the target molecule, or bind only briefly, will not remain near the scintillant long enough to produce a signal above background. Any time spent near the scintillant caused by random Brownian motion will also not result in a significant amount of signal. Likewise, residual unincorporated

radiolabel used during the expression step may be present, but will not generate significant signal because it will be in solution rather than interacting with the target molecule. These non-binding interactions will therefore cause a certain level of background signal that can be mathematically removed. If too many signals are obtained, salt or other modifiers can be added directly to the assay plates until the desired specificity is obtained (Nichols et al., (1998) *Anal. Biochem.* 257:112-119).

Assay Compounds and Molecular Scaffolds

[0263] Preferred characteristics of a scaffold include being of low molecular weight (e.g., less than 350 Da, or from about 100 to about 350 daltons, or from about 150 to about 300 daltons). Preferably clog P of a scaffold is from –1 to 8, more preferably less than 6, 5, or 4, most preferably less than 3. In particular embodiments the clogP is in a range –1 to an upper limit of 2, 3, 4, 5, 6, or 8; or is in a range of 0 to an upper limit of 2,3, 4, 5, 6, or 8. Preferably the number of rotatable bonds is less than 5, more preferably less than 4. Preferably the number of hydrogen bond donors and acceptors is below 6, more preferably below 5. An additional criterion that can be useful is a polar surface area of less than 5. Guidance that can be useful in identifying criteria for a particular application can be found in Lipinski et al., (1997) *Advanced Drug Delivery Reviews* 23 3-25, which is hereby incorporated by reference in its entirety.

[0264] A scaffold may preferably bind to a given protein binding site in a configuration that causes substituent moieties of the scaffold to be situated in pockets of the protein binding site. Also, possessing chemically tractable groups that can be chemically modified, particularly through synthetic reactions, to easily create a combinatorial library can be a preferred characteristic of the scaffold. Also preferred can be having positions on the scaffold to which other moieties can be attached, which do not interfere with binding of the scaffold to the protein(s) of interest but do cause the scaffold to achieve a desirable property, for example, active transport of the scaffold to cells and/or organs, enabling the scaffold to be attached to a chromatographic column to facilitate analysis, or another desirable property. A molecular scaffold can bind to a target molecule with any affinity, such as binding at high affinity, moderate affinity, low affinity, very low affinity, or extremely low affinity.

[0265] Thus, the above criteria can be utilized to select many compounds for testing that have the desired attributes. Many compounds having the criteria described are available in the commercial market, and may be selected for assaying depending on the specific needs to which the methods are to be applied.

[0266] A "compound library" or "library" is a collection of different compounds having different chemical structures. A compound library is screenable, that is, the compound library members therein may be subject to screening assays. In preferred embodiments, the library members can have a molecular weight of from about 100 to about 350 daltons, or from about 150 to about 350 daltons. Examples of libraries are provided above.

[0267] Libraries of the present invention can contain at least one compound than binds to the target molecule at low affinity. Libraries of candidate compounds can be assayed by many different assays, such as those described above, e.g., a fluorescence polarization assay. Libraries may consist of chemically synthesized peptides, peptidomimetics, or arrays of combinatorial chemicals that are large or small, focused or nonfocused. By "focused" it is meant that the collection of compounds is prepared using the structure of previously characterized compounds and/or pharmacophores.

[0268] Compound libraries may contain molecules isolated from natural sources, artificially synthesized molecules, or molecules synthesized, isolated, or otherwise prepared in such a manner so as to have one or more moieties variable, e.g., moieties that are independently isolated or randomly synthesized. Types of molecules in compound libraries include but are not limited to organic compounds, polypeptides and nucleic acids as those terms are used herein, and derivatives, conjugates and mixtures thereof.

[0269] Compound libraries of the invention may be purchased on the commercial market or prepared or obtained by any means including, but not limited to, combinatorial chemistry techniques, fermentation methods, plant and cellular extraction procedures and the like (see, e.g., Cwirla et al., (1990) *Biochemistry*, 87, 6378-6382; Houghten et al., (1991) *Nature*, 354, 84-86; Lam et al., (1991) *Nature*, 354, 82-84; Brenner et al., (1992) *Proc. Natl. Acad. Sci. USA*, 89, 5381-5383; R. A. Houghten, (1993) *Trends Genet.*, 9, 235-239; E. R. Felder, (1994) *Chimia*, 48, 512-541; Gallop et al., (1994) *J. Med. Chem.*, 37, 1233-1251; Gordon et al., (1994) *J. Med. Chem.*; 37, 1385-1401; Carell et al., (1995) *Chem. Biol.*, 3, 171-183; Madden et al., *Perspectives in Drug Discovery and Design* 2,

269-282; Lebl et al., (1995) *Biopolymers*, 37 177-198); small molecules assembled around a shared molecular structure; collections of chemicals that have been assembled by various commercial and noncommercial groups, natural products; extracts of marine organisms, fungi, bacteria, and plants.

[0270] Preferred libraries can be prepared in a homogenous reaction mixture, and separation of unreacted reagents from members of the library is not required prior to screening. Although many combinatorial chemistry approaches are based on solid state chemistry, liquid phase combinatorial chemistry is capable of generating libraries (Sun CM., (1999) Recent advances in liquid-phase combinatorial chemistry, *Combinatorial Chemistry & High Throughput Screening*. 2:299-318).

[0271] Libraries of a variety of types of molecules are prepared in order to obtain members therefrom having one or more preselected attributes that can be prepared by a variety of techniques, including but not limited to parallel array synthesis (Houghton, (2000) *Annu Rev Pharmacol Toxicol* 40:273-82, Parallel array and mixture-based synthetic combinatorial chemistry; solution-phase combinatorial chemistry (Merritt, (1998) *Comb Chem High Throughput Screen* 1(2):57-72, Solution phase combinatorial chemistry, Coe et al., (1998-99) *Mol Divers*;4(1):31-8, Solution-phase combinatorial chemistry, Sun, (1999) *Comb Chem High Throughput Screen* 2(6):299-318, Recent advances in liquid-phase combinatorial chemistry); synthesis on soluble polymer (Gravert et al., (1997) *Curr Opin Chem Biol* 1(1):107-13, Synthesis on soluble polymers: new reactions and the construction of small molecules); and the like. See, e.g., Dolle et al., (1999) *J Comb Chem* 1(4):235-82, Comprehensive survey of cominatorial library synthesis: 1998. Freidinger RM., (1999) Nonpeptidic ligands for peptide and protein receptors, Current Opinion in Chemical Biology; and Kundu et al., *Prog Drug Res*;53:89-156, Combinatorial chemistry: polymer supported synthesis of peptide and non-peptide libraries). Compounds may be clinically tagged for ease of identification (Chabala, (1995) *Curr Opin Biotechnol* 6(6):633-9, Solid-phase combinatorial chemistry and novel tagging methods for identifying leads).

[0272] The combinatorial synthesis of carbohydrates and libraries containing oligosaccharides have been described (Schweizer et al., (1999) *Curr* Opin *Chem Biol* 3(3):291-8, Combinatorial synthesis of carbohydrates). The synthesis of natural-product

based compound libraries has been described (Wessjohann, (2000) *Curr Opin Chem Biol* 4(3):303-9, Synthesis of natural-product based compound libraries).

[0273] Libraries of nucleic acids are prepared by various techniques, including by way of non-limiting example the ones described herein, for the isolation of aptamers. Libraries that include oligonucleotides and polyaminooligonucleotides (Markiewicz et al., (2000) Synthetic oligonucleotide combinatorial libraries and their applications, *Farmaco.* 55:174-7) displayed on streptavidin magnetic beads are known. Nucleic acid libraries are known that can be coupled to parallel sampling and be deconvoluted without complex procedures such as automated mass spectrometry (Enjalbal C. Martinez J. Aubagnac JL, (2000) Mass spectrometry in combinatorial chemistry, *Mass Spectrometry Reviews.* 19:139-61) and parallel tagging. (Perrin DM., Nucleic acids for recognition and catalysis: landmarks, limitations, and looking to the future, *Combinatorial Chemistry & High Throughput Screening* 3:243-69).

[0274] Peptidomimetics are identified using combinatorial chemistry and solid phase synthesis (Kim HO. Kahn M., (2000) A merger of rational drug design and combinatorial chemistry: development and application of peptide secondary structure mimetics, Combinatorial Chemistry & High Throughput Screening 3:167-83; al-Obeidi, (1998) *Mol Biotechnol* 9(3):205-23, Peptide and peptidomimetric libraries. Molecular diversity and drug design). The synthesis may be entirely random or based in part on a known polypeptide.

[0275] Polypeptide libraries can be prepared according to various techniques. In brief, phage display techniques can be used to produce polypeptide ligands (Gram H., (1999) Phage display in proteolysis and signal transduction, Combinatorial Chemistry & High Throughput Screening. 2:19-28) that may be used as the basis for synthesis of peptidomimetics. Polypeptides, constrained peptides, proteins, protein domains, antibodies, single chain antibody fragments, antibody fragments, and antibody combining regions are displayed on filamentous phage for selection.

[0276] Large libraries of individual variants of human single chain Fv antibodies have been produced. See, e.g., Siegel RW. Allen B. Pavlik P. Marks JD. Bradbury A., (2000) Mass spectral analysis of a protein complex using single-chain antibodies selected on a peptide target: applications to functional genomics, *Journal of Molecular Biology*

302:285-93; Poul MA. Becerril B. Nielsen UB. Morisson P. Marks JD.,(2000) Selection of tumor-specific internalizing human antibodies from phage libraries. Source *Journal of Molecular Biology*. 301:1149-61; Amersdorfer P. Marks JD., (2001) Phage libraries for generation of anti-botulinum scFv antibodies, *Methods in Molecular Biology*. 145:219-40; Hughes-Jones NC. Bye JM. Gorick BD. Marks JD. Ouwehand WH., (1999) Synthesis of Rh Fv phage-antibodies using VH and VL germline genes, *British Journal of Haematology*. 105:811-6; McCall AM. Amoroso AR. Sautes C. Marks JD. Weiner LM., (1998) Characterization of anti-mouse Fc gamma RII single-chain Fv fragments derived from human phage display libraries, *Immunotechnology*. 4:71-87; Sheets MD. Amersdorfer P. Finnern R. Sargent P. Lindquist E. Schier R. Hemingsen G. Wong C. Gerhart JC. Marks JD. Lindquist E., (1998) Efficient construction of a large nonimmune phage antibody library: the production of high-affinity human single-chain antibodies to protein antigens (published erratum appears in *Proc Natl Acad Sci* USA 1999 96:795), *Proc Natl Acad Sci USA* 95:6157-62).

[0277] Focused or smart chemical and pharmacophore libraries can be designed with the help of sophisticated strategies involving computational chemistry (e.g., Kundu B. Khare SK. Rastogi SK., (1999) Combinatorial chemistry: polymer supported synthesis of peptide and non-peptide libraries, *Progress in Drug Research* 53:89-156) and the use of structure-based ligands using database searching and docking, de novo drug design and estimation of ligand binding affinities (Joseph-McCarthy D., (1999) Computational approaches to structure-based ligand design, *Pharmacology & Therapeutics* 84:179-91; Kirkpatrick DL. Watson S. Ulhaq S., (1999) Structure-based drug design: combinatorial chemistry and molecular modeling, *Combinatorial Chemistry & High Throughput Screening*. 2:211-21; Eliseev AV. Lehn JM., (1999) Dynamic combinatorial chemistry: evolutionary formation and screening of molecular libraries, *Current Topics in Microbiology & Immunology* 243:159-72; Bolger et al., (1991) *Methods Enz.* 203:21-45; Martin, (1991) *Methods Enz.* 203:587-613; Neidle et al., (1991) *Methods Enz.* 203:433-458; U.S. Patent 6,178,384).

X. Crystallography

[0278] After binding compounds have been determined, the orientation of compound bound to target is determined. Preferably this determination involves crystallography on co-crystals of molecular scaffold compounds with target. Most protein crystallographic

platforms can preferably be designed to analyze up to about 500 co-complexes of compounds, ligands, or molecular scaffolds bound to protein targets due to the physical parameters of the instruments and convenience of operation. If the number of scaffolds that have binding activity exceeds a number convenient for the application of crystallography methods, the scaffolds can be placed into groups based on having at least one common chemical structure or other desirable characteristics, and representative compounds can be selected from one or more of the classes. Classes can be made with increasingly exacting criteria until a desired number of classes (e.g., 500) is obtained. The classes can be based on chemical structure similarities between molecular scaffolds in the class, e.g., all possess a pyrrole ring, benzene ring, or other chemical feature. Likewise, classes can be based on shape characteristics, e.g., space-filling characteristics.

[0279] The co-crystallography analysis can be performed by co-complexing each scaffold with its target at concentrations of the scaffold that showed activity in the screening assay. This co-complexing can be accomplished with the use of low percentage organic solvents with the target molecule and then concentrating the target with each of the scaffolds. In preferred embodiments these solvents are less than 5% organic solvent such as dimethyl sulfoxide (DMSO), ethanol, methanol, or ethylene glycol in water or another aqueous solvent. Each scaffold complexed to the target molecule can then be screened with a suitable number of crystallization screening conditions at both 4 and 20 degrees. In preferred embodiments, about 96 crystallization screening conditions can be performed in order to obtain sufficient information about the co-complexation and crystallization conditions, and the orientation of the scaffold at the binding site of the target molecule. Crystal structures can then be analyzed to determine how the bound scaffold is oriented physically within the binding site or within one or more binding pockets of the molecular family member.

[0280] It is desirable to determine the atomic coordinates of the compounds bound to the target proteins in order to determine which is a most suitable scaffold for the protein family. X-ray crystallographic analysis is therefore most preferable for determining the atomic coordinates. Those compounds selected can be further tested with the application of medicinal chemistry. Compounds can be selected for medicinal chemistry testing based on their binding position in the target molecule. For example, when the compound binds at a binding site, the compound's binding position in the binding site of the target

molecule can be considered with respect to the chemistry that can be performed on chemically tractable structures or sub-structures of the compound, and how such modifications on the compound might interact with structures or sub-structures on the binding site of the target. Thus, one can explore the binding site of the target and the chemistry of the scaffold in order to make decisions on how to modify the scaffold to arrive at a ligand with higher potency and/or selectivity. This process allows for more direct design of ligands, by utilizing structural and chemical information obtained directly from the co-complex, thereby enabling one to more efficiently and quickly design lead compounds that are likely to lead to beneficial drug products. In various embodiments it may be desirable to perform co-crystallography on all scaffolds that bind, or only those that bind with a particular affinity, for example, only those that bind with high affinity, moderate affinity, low affinity, very low affinity, or extremely low affinity. It may also be advantageous to perform co-crystallography on a selection of scaffolds that bind with any combination of affinities.

[0281] Standard X-ray protein diffraction studies such as by using a Rigaku RU-200® (Rigaku, Tokyo, Japan) with an X-ray imaging plate detector or a synchrotron beam-line can be performed on co-crystals and the diffraction data measured on a standard X-ray detector, such as a CCD detector or an X-ray imaging plate detector.

[0282] Performing X-ray crystallography on about 200 co-crystals should generally lead to about 50 co-crystals structures, which should provide about 10 scaffolds for validation in chemistry, which should finally result in about 5 selective leads for target molecules.

Virtual Assays

[0283] Commercially available software that generates three-dimensional graphical representations of the complexed target and compound from a set of coordinates provided can be used to illustrate and study how a compound is oriented when bound to a target. (e.g., QUANTA®, Accelerys, San Diego, CA). Thus, the existence of binding pockets at the binding site of the targets can be particularly useful in the present invention. These binding pockets are revealed by the crystallographic structure determination and show the precise chemical interactions involved in binding the compound to the binding site of the target. The person of ordinary skill will realize that the illustrations can also be used to decide where chemical groups might be added, substituted, modified, or deleted from the

scaffold to enhance binding or another desirable effect, by considering where unoccupied space is located in the complex and which chemical substructures might have suitable size and/or charge characteristics to fill it. The person of ordinary skill will also realize that regions within the binding site can be flexible and its properties can change as a result of scaffold binding, and that chemical groups can be specifically targeted to those regions to achieve a desired effect. Specific locations on the molecular scaffold can be considered with reference to where a suitable chemical substructure can be attached and in which conformation, and which site has the most advantageous chemistry available.

[0284] An understanding of the forces that bind the compounds to the target proteins reveals which compounds can most advantageously be used as scaffolds, and which properties can most effectively be manipulated in the design of ligands. The person of ordinary skill will realize that steric, ionic, hydrogen bond, and other forces can be considered for their contribution to the maintenance or enhancement of the target-compound complex. Additional data can be obtained with automated computational methods, such as docking and/or Free Energy Perturbations (FEP), to account for other energetic effects such as desolvation penalties. The compounds selected can be used to generate information about the chemical interactions with the target or for elucidating chemical modifications that can enhance selectivity of binding of the compound.

[0285] Computer models, such as homology models (*i.e.*, based on a known, experimentally derived structure) can be constructed using data from the co-crystal structures. When the target molecule is a protein or enzyme, preferred co-crystal structures for making homology models contain high sequence identity in the binding site of the protein sequence being modeled, and the proteins will preferentially also be within the same class and/or fold family. Knowledge of conserved residues in active sites of a protein class can be used to select homology models that accurately represent the binding site. Homology models can also be used to map structural information from a surrogate protein where an apo or co-crystal structure exists to the target protein.

[0286] Virtual screening methods, such as docking, can also be used to predict the binding configuration and affinity of scaffolds, compounds, and/or combinatorial library members to homology models. Using this data, and carrying out "virtual experiments" using computer software can save substantial resources and allow the person of ordinary

skill to make decisions about which compounds can be suitable scaffolds or ligands, without having to actually synthesize the ligand and perform co-crystallization. Decisions thus can be made about which compounds merit actual synthesis and co-crystallization. An understanding of such chemical interactions aids in the discovery and design of drugs that interact more advantageously with target proteins and/or are more selective for one protein family member over others. Thus, applying these principles, compounds with superior properties can be discovered.

[0287] Additives that promote co-crystallization can of course be included in the target molecule formulation in order to enhance the formation of co-crystals. In the case of proteins or enzymes, the scaffold to be tested can be added to the protein formulation, which is preferably present at a concentration of approximately 1 mg/ml. The formulation can also contain between 0%-10% (v/v) organic solvent, e.g. DMSO, methanol, ethanol, propane diol, or 1,3 dimethyl propane diol (MPD) or some combination of those organic solvents. Compounds are preferably solubilized in the organic solvent at a concentration of about 10 mM and added to the protein sample at a concentration of about 100 mM. The protein-compound complex is then concentrated to a final concentration of protein of from about 5 to about 20 mg/ml. The complexation and concentration steps can conveniently be performed using a 96-well formatted concentration apparatus (e.g., Amicon Inc., Piscataway, NJ). Buffers and other reagents present in the formulation being crystallized can contain other components that promote crystallization or are compatible with crystallization conditions, such as DTT, propane diol, glycerol.

[0288] The crystallization experiment can be set-up by placing small aliquots of the concentrated protein-compound complex (1 μl) in a 96 well format and sampling under 96 crystallization conditions. (Other screening formats can also be used, *e.g.*, plates with greater than 96 wells.) Crystals can typically be obtained using standard crystallization protocols that can involve the 96 well crystallization plate being placed at different temperatures. Co-crystallization varying factors other than temperature can also be considered for each protein-compound complex if desirable. For example, atmospheric pressure, the presence or absence of light or oxygen, a change in gravity, and many other variables can all be tested. The person of ordinary skill in the art will realize other variables that can advantageously be varied and considered.

Ligand Design and Preparation

[0289] The design and preparation of ligands can be performed with or without structural and/or co-crystallization data by considering the chemical structures in common between the active scaffolds of a set. In this process structure-activity hypotheses can be formed and those chemical structures found to be present in a substantial number of the scaffolds, including those that bind with low affinity, can be presumed to have some effect on the binding of the scaffold. This binding can be presumed to induce a desired biochemical effect when it occurs in a biological system (e.g., a treated mammal). New or modified scaffolds or combinatorial libraries derived from scaffolds can be tested to disprove the maximum number of binding and/or structure-activity hypotheses. The remaining hypotheses can then be used to design ligands that achieve a desired binding and biochemical effect.

[0290] But in many cases it will be preferred to have co-crystallography data for consideration of how to modify the scaffold to achieve the desired binding effect (e.g., binding at higher affinity or with higher selectivity). Using the case of proteins and enzymes, co-crystallography data shows the binding pocket of the protein with the molecular scaffold bound to the binding site, and it will be apparent that a modification can be made to a chemically tractable group on the scaffold. For example, a small volume of space at a protein binding site or pocket might be filled by modifying the scaffold to include a small chemical group that fills the volume. Filling the void volume can be expected to result in a greater binding affinity, or the loss of undesirable binding to another member of the protein family. Similarly, the co-crystallography data may show that deletion of a chemical group on the scaffold may decrease a hindrance to binding and result in greater binding affinity or specificity.

[0291] It can be desirable to take advantage of the presence of a charged chemical group located at the binding site or pocket of the protein. For example, a positively charged group can be complemented with a negatively charged group introduced on the molecular scaffold. This can be expected to increase binding affinity or binding specificity, thereby resulting in a more desirable ligand. In many cases, regions of protein binding sites or pockets are known to vary from one family member to another based on the amino acid differences in those regions. Chemical additions in such regions can result in the creation or elimination of certain interactions (e.g., hydrophobic, electrostatic, or entropic) that

allow a compound to be more specific for one protein target over another or to bind with greater affinity, thereby enabling one to synthesize a compound with greater selectivity or affinity for a particular family member. Additionally, certain regions can contain amino acids that are known to be more flexible than others. This often occurs in amino acids contained in loops connecting elements of the secondary structure of the protein, such as alpha helices or beta strands. Additions of chemical moieties can also be directed to these flexible regions in order to increase the likelihood of a specific interaction occurring between the protein target of interest and the compound. Virtual screening methods can also be conducted *in silico* to assess the effect of chemical additions, subtractions, modifications, and/or substitutions on compounds with respect to members of a protein family or class.

[0292] The addition, subtraction, or modification of a chemical structure or sub-structure to a scaffold can be performed with any suitable chemical moiety. For example the following moieties, which are provided by way of example and are not intended to be limiting, can be utilized: hydrogen, alkyl, alkoxy, phenoxy, alkenyl, alkynyl, phenylalkyl, hydroxyalkyl, haloalkyl, aryl, arylalkyl, alkyloxy, alkylthio, alkenylthio, phenyl, phenylalkyl, phenylalkylthio, hydroxyalkyl-thio, alkylthiocarbbamylthio, cyclohexyl, pyridyl, piperidinyl, alkylamino, amino, nitro, mercapto, cyano, hydroxyl, a halogen atom, halomethyl, an oxygen atom (e.g., forming a ketone or N-oxide) or a sulphur atom (e.g., forming a thiol, thione, di-alkylsulfoxide or sulfone) are all examples of moieties that can be utilized.

[0293] Additional examples of structures or sub-structures that may be utilized are an aryl optionally substituted with one, two, or three substituents independently selected from the group consisting of alkyl, alkoxy, halogen, trihalomethyl, carboxylate, carboxamide, nitro, and ester moieties; an amine of formula $-NX_2X_3$, where X_2 and X_3 are independently selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and homocyclic or heterocyclic ring moieties; halogen or trihalomethyl; a ketone of formula $-COX_4$, where X_4 is selected from the group consisting of alkyl and homocyclic or heterocyclic ring moieties; a carboxylic acid of formula $-(X_5)_nCOOH$ or ester of formula $(X_6)_nCOOX_7$, where X_5, X_6, and X_7 and are independently selected from the group consisting of alkyl and homocyclic or heterocyclic ring moieties and where n is 0 or 1; an alcohol of formula $(X_8)_nOH$ or an alkoxy moiety of formula $-(X_8)_nOX_9$, where X_8 and X_9

are independently selected from the group consisting of saturated or unsaturated alkyl and homocyclic or heterocyclic ring moieties, wherein said ring is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkoxy, halogen, trihalomethyl, carboxylate, nitro, and ester and where n is 0 or 1; an amide of formula $NHCOX_{10}$, where X_{10} is selected from the group consisting of alkyl, hydroxyl, and homocyclic or heterocyclic ring moieties, wherein said ring is optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkoxy, halogen, trihalomethyl, carboxylate, nitro, and ester; SO_2, NX_{11} X_{12}, where X_{11} and X_{12} are selected from the group consisting of hydrogen, alkyl, and homocyclic or heterocyclic ring moieties; a homocyclic or heterocyclic ring moiety optionally substituted with one, two, or three substituents independently selected from the group consisting of alkyl, alkoxy, halogen, trihalomethyl, carboxylate, carboxamide, nitro, and ester moieties; an aldehyde of formula -CHO; a sulfone of formula $-SO_2X_{13}$, where X_{13} is selected from the group consisting of saturated or unsaturated alkyl and homocyclic or heterocyclic ring moieties; and a nitro of formula $-NO_2$.

Identification of Attachment Sites on Molecular Scaffolds and Ligands

[0294] In addition to the identification and development of ligands for kinases and other enzymes, determination of the orientation of a molecular scaffold or other binding compound in a binding site allows identification of energetically allowed sites for attachment of the binding molecule to another component. For such sites, any free energy change associated with the presence of the attached component should not destablize the binding of the compound to the kinase to an extent that will disrupt the binding. Preferably, the binding energy with the attachment should be at least 4 kcal/mol., more preferably at least 6, 8, 10, 12, 15, or 20 kcal/mol. Preferably, the presence of the attachment at the particular site reduces binding energy by no more than 3, 4, 5, 8, 10, 12, or 15 kcal/mol.

[0295] In many cases, suitable attachment sites will be those that are exposed to solvent when the binding compound is bound in the binding site. In some cases, attachment sites can be used that will result in small displacements of a portion of the enzyme without an excessive energetic cost. Exposed sites can be identified in various ways. For example, exposed sites can be identified using a graphic display or 3-dimensional model. In a grahic display, such as a computer display, an image of a compound bound in a binding

site can be visually inspected to reveal atoms or groups on the compound that are exposed to solvent and oriented such that attachment at such atom or group would not preclude binding of the enzyme and binding compound. Energetic costs of attachment can be calculated based on changes or distortions that would be caused by the attachment as well as entropic changes.

[0296] Many different types of components can be attached. Persons with skill are familiar with the chemistries used for various attachments. Examples of components that can be attached include, without limitation: solid phase components such as beads, plates, chips, and wells; a dlrect or indirect label; a linker, which may be a traceless linker; among others. Such linkers can themselves be attached to other components, *e.g.*, to solid phase media, labels, and/or binding moieties.

[0297] The binding energy of a compound and the effects on binding energy for attaching the molecule to another component can be calculated approximately using any of a variety of available software or by manual calculation. An example is the following:

[0298] Calculations were performed to estimate binding energies of different organic molecules to two Kinases: PIM-1 and CDK2. The organic molecules considered included Staurosporine, identified compounds that bind to PIM-1, and several linkers.

[0299] Calculated binding energies between protein-ligand complexes were obtained using the FlexX score (an implementation of the Bohm scoring function) within the Tripos software suite. The form for that equation is shown in Eqn. 1 below:

$$\Delta G_{bind} = \Delta G_{tr} + \Delta G_{hb} + \Delta G_{ion} + \Delta G_{lipo} + \Delta G_{arom} + \Delta G_{rot}$$

[0300] where: ΔG_{tr} is a constant term that accounts for the overall loss of rotational and translational entropy of the lignand, ΔG_{hb} accounts for hydrogen bonds formed between the ligand and protein, ΔG_{ion} accounts for the ionic interactions between the ligand and protein, ΔG_{lipo} accounts for the lipophilic interaction that corresponds to the protein-ligand contact surface, ΔG_{arom} accounts for interactions between aromatic rings in the protein and ligand, and ΔG_{rot} accounts for the entropic penalty of restricting rotatable bonds in the ligand upon binding.

[0301] This method estimates the free energy that a lead compound should have to a target protein for which there is a crystal structure, and it accounts for the entropic penalty of flexible linkers. It can therefore be used to estimate the free energy penalty incurred by attaching linkers to molecules being screened and the binding energy that a lead compound should have in order to overcome the free energy penalty of the linker. The method does not account for solvation and the entropic penalty is likely overestimated for cases where the linker is bound to a solid phase through another binding complex, such as a biotin:streptavidin complex.

[0302] Co-crystals were aligned by superimposing residues of PIM-1 with corresponding residues in CDK2. The PIM-1 structure used for these calculations was a co-crystal of PYK2 with a binding compound. The CDK2:Staurosporine co-crystal used was from the Brookhaven database file 1aq1. Hydrogen atoms were added to the proteins and atomic charges were assigned using the AMBER95 parameters within Sybyl. Modifications to the compounds described were made within the Sybyl modeling suite from Tripos.

[0303] These calcualtions indicate that the calculated binding energy for compounds that bind strongly to a given target (such as Staurosporine:CDK2) can be lower than –25 kcal/mol, while the calculated binding affinity for a good scaffold or an unoptimized binding compound can be in the range of -15 to -20. The free energy penalty for attachment to a linker such as the ethylene glycol or hexatriene is estimated as typically being in the range of +5 to +15 kcal/mol.

Linkers

[0304] Linkers suitable for use in the invention can be of many different types. Linkers can be selected for particular applications based on factors such as linker chemistry compatible for attachment to a binding compound and to another component utilized in the particular application. Additional factors can include, without limitation, linker length, linker stability, and ability to remove the linker at an appropriate time. Exemplary linkers include, but are not limited to, hexyl, hexatrienyl, ethylene glycol, and peptide linkers. Traceless linkers can also be used, *e.g.*, as described in Plunkett, M. J., and Ellman, J. A., (1995), *J. Org. Chem.*, 60:6006.

[0305] Typical functional groups, that are utilized to link binding compound(s), include, but not limited to, carboxylic acid, amine, hydroxyl, and thiol. (Examples can be found in Solid-supported combinatorial and parallel synthesis of small molecular weight compound libraries; (1998) Tetrahedron organic chemistry series Vol.17; Pergamon; p85).

Labels

[0306] As indicated above, labels can also be attached to a binding compound or to a linker attached to a binding compound. Such attachment may be direct (attached directly to the binding compound) or indirect (attached to a component that is directly or indirectly attached to the binding compound). Such labels allow detection of the compound either directly or indirectly. Attachement of labels can be performed using conventional chemistries. Labels can include, for example, fluorescent labels, radiolabels, light scattering particles, light absorbent particles, magnetic particles, enzymes, and specific binding agents (*e.g.*, biotin or an antibody target moiety).

Solid Phase Media

[0307] Additional examples of components that can be attached directly or indirectly to a binding compound include various solid phase media. Similar to attachment of linkers and labels, attachment to solid phase media can be performed using conventional chemistries. Such solid phase media can include, for example, small components such as beads, nanoparticles, and fibers (*e.g.*, in suspension or in a gel or chromatographic matrix). Likewise, solid phase media can include larger objects such as plates, chips, slides, and tubes. In many cases, the binding compound will be attached in only a portion of such an objects, *e.g.*, in a spot or other local element on a generally flat surface or in a well or portion of a well.

Identification of Biological Agents

[0308] The posession of structural information about a protein also provides for the identification of useful biological agents, such as epitpose for development of antibodies, identification of mutation sites expected to affect activity, and identification of attachment sites allowing attachment of the protein to materials such as labels, linkers, peptides, and solid phase media.

[0309] Antibodies (Abs) finds multiple applications in a variety of areas including biotechnology, medicine and diagnosis, and indeed they are one of the most powerful tools for life science research. Abs directed against protein antigens can recognize either linear or native three-dimensional (3D) epitopes. The obtention of Abs that recognize 3D epitopes require the use of whole native protein (or of a portion that assumes a native conformation) as immunogens. Unfortunately, this not always a choice due to various technical reasons: for example the native protein is just not available, the protein is toxic, or its is desirable to utilize a high density antigen presentation. In such cases, immunization with peptides is the alternative. Of course, Abs generated in this manner will recognize linear epitopes, and they might or might not recognize the source native protein, but yet they will be useful for standard laboratory applications such as western blots. The selection of peptides to use as immunogens can be accomplished by following particular selection rules and/or use of epitope prediction software.

[0310] Though methods to predict antigenic peptides are not infallible, there are several rules that can be followed to determine what peptide fragments from a protein are likely to be antigenic. These rules are also dictated to increase the likelihood that an Ab to a particular peptide will recognize the native protein.

- 1. Antigenic peptides should be located in solvent accessible regions and contain both hydrophobic and hydrophilic residues.
    - For proteins of known 3D structure, solvent accessibility can be determined using a variety of programs such as DSSP, NACESS, or WHATIF, among others.
    - If the 3D structure is not known, use any of the following web servers to predict accessibilities: PHD, JPRED, PredAcc (c) ACCpro
- 2. Preferably select peptides lying in long loops connecting Secondary Structure (SS) motifs, avoiding peptides located in helical regions. This will increase the odds that the Ab recognizes the native protein. Such peptides can, for example, be identified from a crystal structure or crystal structure-based homology model.

- For protein with known 3D coordinates, SS can be obtained from the sequence link of the relevant entry at the Brookhaven data bank. The PDBsum server also offer SS analysis of pdb records.
- When no structure is available secondary structure predictions can be obtained from any of the following servers: PHD, JPRED, PSI-PRED, NNSP, etc

- 3. When possible, choose peptides that are in the N- and C-terminal region of the protein. Because the N- and C- terminal regions of proteins are usually solvent accessible and unstructured, Abs against those regions are also likely to recognize the native protein.
- 4. For cell surface glycoproteins, eliminate from initial peptides those containing consesus sites for N-glycosilation.
  - N-glycosilation sites can be detected using Scanprosite, or NetNGlyc

[0311] In addition, several methods based on various physio-chemical properties of experimental determined epitopes (flexibility, hydrophibility, accessibility) have been published for the prediction of antigenic determinants and can be used. The antigenic index and Preditop are example.

[0312] Perhaps the simplest method for the prediction of antigenic determinants is that of Kolaskar and Tongaonkar, which is based on the occurrence of amino acid residues in experimentally determined epitopes. (Kolaskar and Tongaonkar (1990) A semi-empirical method for prediction of antigenic determinants on protein antigens. *FEBBS Lett.* 276(1-2):172-174.) The prediction algorithm works as follows:

- 1. Calculate the average propensity for each overlapping 7-mer and assign the result to the central residue (i+3) of the 7-mer.
- 2. Calculate the average for the whole protein.
- 3. (a) If the average for the whole protein is above 1.0 then all residues having average propensity above 1.0 are potentially antigenic.

- 3. (b) If the average for the whole protein is below 1.0 then all residues having above the average for the whole protein are potentially antigenic.
- 4. Find 8-mers where all residues are selected by step 3 above (6-mers in the original paper)

[0313] The Kolaskar and Tongaonkar method is also available from the GCG package, and it runs using the command *egcg*.

[0314] Crystal structures also allow identification of residues at which mutation is likely to alter the activity of the protein. Such residues include, for example, residues that interact with susbtrate, conserved active site residues, and residues that are in a region of ordered secondary structure of involved in tertiary interactions. The mutations that are likely to affect activity will vary for different molecular contexts. Mutations in an active site that will affect activity are typically substitutions or deletions that eliminate a charge-charge or hydrogen bonding interaction, or introduce a steric interference. Mutations in secondary structure regions or molecular interaction regions that are likely to affect activity include, for example, substitutions that alter the hydrophobicity/hydrophilicity of a region, or that introduce a sufficient strain in a region near or including the active site so that critical residue(s) in the active site are displaced. Such substitutions and/or deletions and/or insertions are recognized, and the predicted structural and/or energetic effects of mutations can be calculated using conventional software.

IX. Kinase Activity Assays

[0315] A number of different assays for kinase activity can be utilized for assaying for active modulators and/or determining specificity of a modulator for a particular kinase or group or kinases. In addition to the assays mentioned below, one of ordinary skill in the art will know of other assays that can be utilized and can modify an assay for a particular application.

[0316] An exemplary assay for kinase activity that can be used for PYK2 can be performed according to the following procedure using purified kinase using myelin basic protein (MBP) as substrate. An exemplary assay can use the following materials: MBP (M-1891, Sigma); Kinase buffer (KB = HEPES 50 mM, pH7.2, $MgCl_2$:$MnCl_2$ (200

μM:200 μM); ATP (γ-^{33}P):NEG602H (10 mCi/mL)(Perkin-Elmer); ATP as 100 mM stock in kinase buffer; EDTA as 100 mM stock solution.

[0317] Coat scintillation plate suitable for radioactivity counting (*e.g.*, FlashPlate from Perkin-Elmer, such as the SMP200(basic)) with kinase+MBP mix (final 100 ng+300 ng/well) at 90 -μL/well in kinase buffer. Add compounds at 1 μL/well from 10 mM stock in DMSO. Positive control wells are added with 1 μL of DMSO. Negative control wells are added with 2 μL of EDTA stock solution. ATP solution (10 μL) is added to each well to provide a final concentration of cold ATP is 2 μM, and 50 nCi ATPγ[^{33}P]. The plate is shaken briefly, and a count is taken to initiate count (IC) using an apparatus adapted for counting with the plate selected, *e.g.*, Perkin-Elmer Trilux. Store the plate at 37°C for 4 hrs, then count again to provide final count (FC).

[0318] Net 33P incorporation (NI) is calculated as: NI = FC – IC.

[0319] The effect of the present of a test compound can then be calculated as the percent of the positive control as: %PC = [(NI – NC) / (PC – NC)] x 100, where NC is the net incorporation for the negative control, and PC is the net incorporation for the positive control.

[0320] As indicated above, other assays can also be readily used. For example, kinase activity can be measured on standard polystyrene plates, using biotinylated MBP and ATPγ[^{33}P] and with Streptavidin-coated SPA (scintillation proximity) beads providing the signal.

[0321] Additional alternative assays can employ phospho-specific antibodies as detection reagents with biotinylated peptides as substrates for the kinase. This sort of assay can be formatted either in a fluorescence resonance energy transfer (FRET) format, or using an AlphaScreen (*a*mplified *l*uminescent *p*roximity *h*omogeneous *a*ssay) format by varying the donor and acceptor reagents that are attached to streptavidin or the phosphor-specific antibody.

X. Organic Synthetic Techniques

[0322] The versatility of computer-based modulator design and identification lies in the diversity of structures screened by the computer programs. The computer programs can

search databases that contain very large numbers of molecules and can modify modulators already complexed with the enzyme with a wide variety of chemical functional groups. A consequence of this chemical diversity is that a potential modulator of kinase function may take a chemical form that is not predictable. A wide array of organic synthetic techniques exist in the art to meet the challenge of constructing these potential modulators. Many of these organic synthetic methods are described in detail in standard reference sources utilized by those skilled in the art. One example of suh a reference is March, 1994, Advanced Organic Chemistry; Reactions, Mechanisms and Structure, New York, McGraw Hill. Thus, the techniques useful to synthesize a potential modulator of kinase function identified by computer-based methods are readily available to those skilled in the art of organic chemical synthesis.

XI. Administration

[0323] The methods and compounds will typically be used in therapy for human patients. However, they may also be used to treat similar or identical diseases in other vertebrates such as other primates, sports animals, and pets such as horses, dogs and cats.

[0324] Suitable dosage forms, in part, depend upon the use or the route of administration, for example, oral, transdermal, transmucosal, or by injection (parenteral). Such dosage forms should allow the compound to reach target cells. Other factors are well known in the art, and include considerations such as toxicity and dosage forms that retard the compound or composition from exerting its effects. Techniques and formulations generally may be found in Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Co., Easton, PA, 1990 (hereby incorporated by reference herein).

[0325] Compounds can be formulated as pharmaceutically acceptable salts. Pharmaceutically acceptable salts are non-toxic salts in the amounts and concentrations at which they are administered. The preparation of such salts can facilitate the pharmacological use by altering the physical characteristics of a compound without preventing it from exerting its physiological effect. Useful alterations in physical properties include lowering the melting point to facilitate transmucosal administration and increasing the solubility to facilitate administering higher concentrations of the drug.

[0326] Pharmaceutically acceptable salts include acid addition salts such as those containing sulfate, chloride, hydrochloride, fumarate, maleate, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, cyclohexylsulfamate and quinate. Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, maleic acid, sulfuric acid, phosphoric acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, *p*-toluenesulfonic acid, cyclohexylsulfamic acid, fumaric acid, and quinic acid.

[0327] Pharmaceutically acceptable salts also include basic addition salts such as those containing benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine, procaine, aluminum, calcium, lithium, magnesium, potassium, sodium, ammonium, alkylamine, and zinc, when acidic functional groups, such as carboxylic acid or phenol are present. For example, see Remington's Pharmaceutical Sciences, 19th ed., Mack Publishing Co., Easton, PA, Vol. 2, p. 1457, 1995. Such salts can be prepared using the appropriate corresponding bases.

[0328] Pharmaceutically acceptable salts can be prepared by standard techniques. For example, the free-base form of a compound is dissolved in a suitable solvent, such as an aqueous or aqueous-alcohol in solution containing the appropriate acid and then isolated by evaporating the solution. In another example, a salt is prepared by reacting the free base and acid in an organic solvent.

[0329] The pharmaceutically acceptable salt of the different compounds may be present as a complex. Examples of complexes include 8-chlorotheophylline complex (analogous to, *e.g.*, dimenhydrinate: diphenhydramine 8-chlorotheophylline (1:1) complex; Dramamine) and various cyclodextrin inclusion complexes.

[0330] Carriers or excipients can be used to produce pharmaceutical compositions. The carriers or excipients can be chosen to facilitate administration of the compound. Examples of carriers include calcium carbonate, calcium phosphate, various sugars such as lactose, glucose, or sucrose, or types of starch, cellulose derivatives, gelatin, vegetable oils, polyethylene glycols and physiologically compatible solvents. Examples of physiologically compatible solvents include sterile solutions of water for injection (WFI), saline solution, and dextrose.

[0331] The compounds can be administered by different routes including intravenous, intraperitoneal, subcutaneous, intramuscular, oral, transmucosal, rectal, or transdermal. Oral administration is preferred. For oral administration, for example, the compounds can be formulated into conventional oral dosage forms such as capsules, tablets, and liquid preparations such as syrups, elixirs, and concentrated drops.

[0332] Pharmaceutical preparations for oral use can be obtained, for example, by combining the active compounds with solid excipients, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose (CMC), and/or polyvinylpyrrolidone (PVP: povidone). If desired, disintegrating agents may be added, such as the cross—linked polyvinylpyrrolidone, agar, or alginic acid, or a salt thereof such as sodium alginate.

[0333] Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain, for example, gum arabic, talc, poly-vinylpyrrolidone, carbopol gel, polyethylene glycol (PEG), and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dye-stuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

[0334] Pharmaceutical preparations that can be used orally include push-fit capsules made of gelatin ("gelcaps"), as well as soft, sealed capsules made of gelatin, and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols (PEGs). In addition, stabilizers may be added.

[0335] Alternatively, injection (parenteral administration) may be used, *e.g.*, intramuscular, intravenous, intraperitoneal, and/orsubcutaneous. For injection, the

compounds of the invention are formulated in sterile liquid solutions, preferably in physiologically compatible buffers or solutions, such as saline solution, Hank's solution, or Ringer's solution. In addition, the compounds may be formulated in solid form and redissolved or suspended immediately prior to use. Lyophilized forms can also be produced.

[0336] Administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents may be used to facilitate permeation. Transmucosal administration, for example, may be through nasal sprays or suppositories (rectal or vaginal).

[0337] The amounts of various compound to be administered can be determined by standard procedures taking into account factors such as the compound IC_{50}, the biological half-life of the compound, the age, size, and weight of the patient, and the disorder associated with the patient. The importance of these and other factors are well known to those of ordinary skill in the art. Generally, a dose will be between about 0.01 and 50 mg/kg, preferably 0.1 and 20 mg/kg of the patient being treated. Multiple doses may be used.

Manipulation of PYK2

[0338] As the full-length coding sequence and amino acid sequence of PYK2 is known, cloning, construction of recombinant hPIM-3, production and purification of recombinant protein, introduction of PYK2 into other organisms, and other molecular biological manipulations of PYK2 are readily performed.

[0339] Techniques for the manipulation of nucleic acids, such as, e.g., subcloning, labeling probes (e.g., random-primer labeling using Klenow polymerase, nick translation, amplification), sequencing, hybridization and the like are well disclosed in the scientific and patent literature, see, e.g., Sambrook, ed., Molecular Cloning: a Laboratory Manual (2nd ed.), Vols. 1-3, Cold Spring Harbor Laboratory, (1989); Current Protocols in Molecular Biology, Ausubel, ed. John Wiley & Sons, Inc., New York (1997); Laboratory

Techniques in Biochemistry and Molecular Biology: Hybridization With Nucleic Acid Probes, Part I. Theory and Nucleic Acid Preparation, Tijssen, ed. Elsevier, N.Y. (1993). [0100] Nucleic acid sequences can be amplified as necessary for further use using amplification methods, such as PCR, isothermal methods, rolling circle methods, etc., are well known to the skilled artisan. See, e.g., Saiki, "Amplification of Genomic DNA" in PCR Protocols, Innis et al., Eds., Academic Press, San Diego, CA 1990, pp 13-20; Wharam et al., *Nucleic Acids Res.* 2001 Jun 1;29(11):E54-E54; Hafner et al., *Biotechniques* 2001 Apr;30(4):852-6, 858, 860 passim; Zhong et al., *Biotechniques* 2001 Apr;30(4):852-6, 858, 860 passim.

[0340] Nucleic acids, vectors, capsids, polypeptides, and the like can be analyzed and quantified by any of a number of general means well known to those of skill in the art. These include, e.g., analytical biochemical methods such as NMR, spectrophotometry, radiography, electrophoresis, capillary electrophoresis, high performance liquid chromatography (HPLC), thin layer chromatography (TLC), and hyperdiffusion chromatography, various immunological methods, e.g. fluid or gel precipitin reactions, immunodiffusion, immuno-electrophoresis, radioimmunoassays (RIAs), enzyme-linked immunosorbent assays (ELISAs), immuno-fluorescent assays, Southern analysis, Northern analysis, dot-blot analysis, gel electrophoresis (e.g., SDS-PAGE), nucleic acid or target or signal amplification methods, radiolabeling, scintillation counting, and affinity chromatography.

[0341] Obtaining and manipulating nucleic acids used to practice the methods of the invention can be performed by cloning from genomic samples, and, if desired, screening and re-cloning inserts isolated or amplified from, e.g., genomic clones or cDNA clones. Sources of nucleic acid used in the methods of the invention include genomic or cDNA libraries contained in, e.g., mammalian artificial chromosomes (MACs), see, e.g., U.S. Patent Nos. 5,721,118; 6,025,155; human artificial chromosomes, see, e.g., Rosenfeld (1997) *Nat. Genet.* 15:333-335; yeast artificial chromosomes (YAC); bacterial artificial chromosomes (BAC); P1 artificial chromosomes, see, e.g., Woon (1998) *Genomics* 50:306-316; P1-derived vectors (PACs), see, e.g., Kern (1997) *Biotechniques* 23:120-124; cosmids, recombinant viruses, phages or plasmids. Typically, nucleic acid molecules having a sequence of interest are available from commercial sources and/or from sequence

repositories, or can be obtained using PCR from a suitable cDNA or genomic library, *e.g.*, a library from an appropriate tissue. A number of different such libraries are commercially or publicly available.

[0342] The nucleic acids can be operatively linked to a promoter. A promoter can be one motif or an array of nucleic acid control sequences which direct transcription of a nucleic acid. A promoter can include necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements which can be located as much as several thousand base pairs from the start site of transcription. A "constitutive" promoter is a promoter which is active under most environmental and developmental conditions. An "inducible" promoter is a promoter which is under environmental or developmental regulation. A "tissue specific" promoter is active in certain tissue types of an organism, but not in other tissue types from the same organism. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

[0343] The nucleic acids of the invention can also be provided in expression vectors and cloning vehicles, e.g., sequences encoding the polypeptides of the invention. Expression vectors and cloning vehicles of the invention can comprise viral particles, baculovirus, phage, plasmids, phagemids, cosmids, fosmids, bacterial artificial chromosomes, viral DNA (e.g., vaccinia, adenovirus, foul pox virus, pseudorabies and derivatives of SV40), P1-based artificial chromosomes, yeast plasmids, yeast artificial chromosomes, and any other vectors specific for specific hosts of interest (such as bacillus, *Aspergillus* and yeast). Vectors of the invention can include chromosomal, non-chromosomal and synthetic DNA sequences. Large numbers of suitable vectors are known to those of skill in the art, and are commercially available.

[0344] The nucleic acids of the invention can be cloned, if desired, into any of a variety of vectors using routine molecular biological methods; methods for cloning *in vitro* amplified nucleic acids are disclosed, *e.g.*, U.S. Pat. No. 5,426,039. To facilitate cloning of amplified sequences, restriction enzyme sites can be "built into" a PCR primer pair.

Vectors may be introduced into a genome or into the cytoplasm or a nucleus of a cell and expressed by a variety of conventional techniques, well described in the scientific and patent literature. See, e.g., Roberts (1987) *Nature* 328:731; Schneider (1995) *Protein Expr. Purif.* 6435:10; Sambrook, Tijssen or Ausubel. The vectors can be isolated from natural sources, obtained from such sources as ATCC or GenBank libraries, or prepared by synthetic or recombinant methods. For example, the nucleic acids of the invention can be expressed in expression cassettes, vectors or viruses which are stably or transiently expressed in cells (e.g., episomal expression systems). Selection markers can be incorporated into expression cassettes and vectors to confer a selectable phenotype on transformed cells and sequences. For example, selection markers can code for episomal maintenance and replication such that integration into the host genome is not required.

[0345] The nucleic acids can be administered *in vivo* for *in situ* expression of the peptides or polypeptides of the invention. The nucleic acids can be administered as "naked DNA" (see, e.g., U.S. Patent No. 5,580,859) or in the form of an expression vector, e.g., a recombinant virus. The nucleic acids can be administered by any route, including peri- or intra-tumorally, as described below. Vectors administered *in vivo* can be derived from viral genomes, including recombinantly modified enveloped or non-enveloped DNA and RNA viruses, preferably selected from baculoviridiae, parvoviridiae, picornoviridiae, herpesveridiae, poxviridae, adenoviridiae, or picornnaviridiae. Chimeric vectors may also be employed which exploit advantageous merits of each of the parent vector properties (See e.g., Feng (1997) *Nature Biotechnology* 15:866-870). Such viral genomes may be modified by recombinant DNA techniques to include the nucleic acids of the invention; and may be further engineered to be replication deficient, conditionally replicating or replication competent. In alternative aspects, vectors are derived from the adenoviral (e.g., replication incompetent vectors derived from the human adenovirus genome, see, e.g., U.S. Patent Nos. 6,096,718; 6,110,458; 6,113,913; 5,631,236); adeno-associated viral and retroviral genomes. Retroviral vectors can include those based upon murine leukemia virus (MuLV), gibbon ape leukemia virus (GaLV), Simian Immuno deficiency virus (SIV), human immuno deficiency virus (HIV), and combinations thereof; see, e.g., U.S. Patent Nos. 6,117,681; 6,107,478; 5,658,775; 5,449,614; Buchscher (1992) J. Virol. 66:2731-2739; Johann (1992) *J. Virol.* 66:1635-1640). Adeno-associated virus (AAV)-based vectors can be used to transduce cells with target nucleic acids, e.g., in the *in vitro* production of nucleic acids and peptides, and in *in vivo* and *ex vivo* gene therapy

procedures; see, e.g., U.S. Patent Nos. 6,110,456; 5,474,935; Okada (1996) *Gene Ther.* 3:957-964.

[0346] The present invention also relates to fusion proteins, and nucleic acids encoding them. A polypeptide of the invention can be fused to a heterologous peptide or polypeptide, such as N-terminal identification peptides which impart desired characteristics, such as increased stability or simplified purification. Peptides and polypeptides of the invention can also be synthesized and expressed as fusion proteins with one or more additional domains linked thereto for, e.g., producing a more immunogenic peptide, to more readily isolate a recombinantly synthesized peptide, to identify and isolate antibodies and antibody-expressing B cells, and the like. Detection and purification facilitating domains include, e.g., metal chelating peptides such as polyhistidine tracts and histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp, Seattle WA). The inclusion of a cleavable linker sequences such as Factor Xa or enterokinase (Invitrogen, San Diego CA) between a purification domain and the motif-comprising peptide or polypeptide to facilitate purification. For example, an expression vector can include an epitope-encoding nucleic acid sequence linked to six histidine residues followed by a thioredoxin and an enterokinase cleavage site (see e.g., Williams (1995) *Biochemistry* 34:1787-1797; Dobeli (1998) *Protein Expr. Purif.* 12:404-414). The histidine residues facilitate detection and purification while the enterokinase cleavage site provides a means for purifying the epitope from the remainder of the fusion protein. In one aspect, a nucleic acid encoding a polypeptide of the invention is assembled in appropriate phase with a leader sequence capable of directing secretion of the translated polypeptide or fragment thereof. Technology pertaining to vectors encoding fusion proteins and application of fusion proteins are well disclosed in the scientific and patent literature, see e.g., Kroll (1993) *DNA Cell. Biol.* 12:441-53.

[0347] The nucleic acids and polypeptides of the invention can be bound to a solid support, e.g., for use in screening and diagnostic methods. Solid supports can include, e.g., membranes (e.g., nitrocellulose or nylon), a microtiter dish (e.g., PVC, polypropylene, or polystyrene), a test tube (glass or plastic), a dip stick (e.g., glass, PVC, polypropylene, polystyrene, latex and the like), a microfuge tube, or a glass, silica, plastic,

metallic or polymer bead or other substrate such as paper. One solid support uses a metal (e.g., cobalt or nickel)-comprising column which binds with specificity to a histidine tag engineered onto a peptide.

[0348] Adhesion of molecules to a solid support can be direct (i.e., the molecule contacts the solid support) or indirect (a "linker" is bound to the support and the molecule of interest binds to this linker). Molecules can be immobilized either covalently (e.g., utilizing single reactive thiol groups of cysteine residues (see, e.g., Colliuod (1993) *Bioconjugate Chem.* 4:528-536) or non-covalently but specifically (e.g., via immobilized antibodies (see, e.g., Schuhmann (1991) *Adv. Mater.* 3:388-391; Lu (1995) *Anal. Chem.* 67:83-87; the biotin/strepavidin system (see, e.g., Iwane (1997) *Biophys. Biochem. Res.* Comm. 230:76-80); metal chelating, e.g., Langmuir-Blodgett films (see, e.g., Ng (1995) *Langmuir* 11:4048-55); metal-chelating self-assembled monolayers (see, e.g., Sigal (1996) *Anal. Chem.* 68:490-497) for binding of polyhistidine fusions.

[0349] Indirect binding can be achieved using a variety of linkers which are commercially available. The reactive ends can be any of a variety of functionalities including, but not limited to: amino reacting ends such as N-hydroxysuccinimide (NHS) active esters, imidoesters, aldehydes, epoxides, sulfonyl halides, isocyanate, isothiocyanate, and nitroaryl halides; and thiol reacting ends such as pyridyl disulfides, maleimides, thiophthalimides, and active halogens. The heterobifunctional crosslinking reagents have two different reactive ends, e.g., an amino-reactive end and a thiol-reactive end, while homobifunctional reagents have two similar reactive ends, e.g., bismaleimidohexane (BMH) which permits the cross-linking of sulfhydryl-containing compounds. The spacer can be of varying length and be aliphatic or aromatic. Examples of commercially available homobifunctional cross-linking reagents include, but are not limited to, the imidoesters such as dimethyl adipimidate dihydrochloride (DMA); dimethyl pimelimidate dihydrochloride (DMP); and dimethyl suberimidate dihydrochloride (DMS). Heterobifunctional reagents include commercially available active halogen-NHS active esters coupling agents such as N-succinimidyl bromoacetate and N-succinimidyl (4-iodoacetyl)aminobenzoate (SIAB) and the sulfosuccinimidyl derivatives such as sulfosuccinimidyl(4-iodoacetyl)aminobenzoate (sulfo-SIAB) (Pierce). Another group of coupling agents is the heterobifunctional and thiol cleavable agents

such as N-succinimidyl 3-(2-pyridyidithio)propionate (SPDP) (Pierce Chemicals, Rockford, IL).

[0350] Antibodies can also be used for binding polypeptides and peptides of the invention to a solid support. This can be done directly by binding peptide-specific antibodies to the column or it can be done by creating fusion protein chimeras comprising motif-containing peptides linked to, e.g., a known epitope (e.g., a tag (e.g., FLAG, myc) or an appropriate immunoglobulin constant domain sequence (an "immunoadhesin," see, e.g., Capon (1989) *Nature* 377:525-531 (1989).

[0351] Nucleic acids or polypeptides of the invention can be immobilized to or applied to an array. Arrays can be used to screen for or monitor libraries of compositions (e.g., small molecules, antibodies, nucleic acids, etc.) for their ability to bind to or modulate the activity of a nucleic acid or a polypeptide of the invention. For example, in one aspect of the invention, a monitored parameter is transcript expression of a gene comprising a nucleic acid of the invention. One or more, or, all the transcripts of a cell can be measured by hybridization of a sample comprising transcripts of the cell, or, nucleic acids representative of or complementary to transcripts of a cell, by hybridization to immobilized nucleic acids on an array, or "biochip." By using an "array" of nucleic acids on a microchip, some or all of the transcripts of a cell can be simultaneously quantified. Alternatively, arrays comprising genomic nucleic acid can also be used to determine the genotype of a newly engineered strain made by the methods of the invention. Polypeptide arrays" can also be used to simultaneously quantify a plurality of proteins.

[0352] The terms "array" or "microarray" or "biochip" or "chip" as used herein is a plurality of target elements, each target element comprising a defined amount of one or more polypeptides (including antibodies) or nucleic acids immobilized onto a defined area of a substrate surface. In practicing the methods of the invention, any known array and/or method of making and using arrays can be incorporated in whole or in part, or variations thereof, as disclosed, for example, in U.S. Patent Nos. 6,277,628; 6,277,489; 6,261,776; 6,258,606; 6,054,270; 6,048,695; 6,045,996; 6,022,963; 6,013,440; 5,965,452; 5,959,098; 5,856,174; 5,830,645; 5,770,456; 5,632,957; 5,556,752; 5,143,854; 5,807,522; 5,800,992; 5,744,305; 5,700,637; 5,556,752; 5,434,049; see also, e.g., WO 99/51773; WO 99/09217; WO 97/46313; WO 96/17958; see also, e.g., Johnston (1998) *Curr. Biol.* 8:R171-R174;

Schummer (1997) *Biotechniques* 23:1087-1092; Kern (1997) *Biotechniques* 23:120-124; Solinas-Toldo (1997) *Genes, Chromosomes & Cancer* 20:399-407; Bowtell (1999) *Nature Genetics Supp.* 21:25-32. See also published U.S. patent applications Nos. 20010018642; 20010019827; 20010016322; 20010014449; 20010014448; 20010012537; 20010008765.

Host Cells and Transformed Cells

[0353] The invention also provides a transformed cell comprising a nucleic acid sequence of the invention, *e.g.*, a sequence encoding a polypeptide of the invention, or a vector of the invention. The host cell may be any of the host cells familiar to those skilled in the art, including prokaryotic cells, eukaryotic cells, such as bacterial cells, fungal cells, yeast cells, mammalian cells, insect cells, or plant cells. Exemplary bacterial cells include *E. coli*, *Streptomyces*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*. Exemplary insect cells include *Drosophila* S2 and *Spodoptera* Sf9. Exemplary animal cells include CHO, COS or Bowes melanoma or any mouse or human cell line. The selection of an appropriate host is within the abilities of those skilled in the art.

[0354] Vectors may be introduced into the host cells using any of a variety of techniques, including transformation, transfection, transduction, viral infection, gene guns, or Ti-mediated gene transfer. Particular methods include calcium phosphate transfection, DEAE-Dextran mediated transfection, lipofection, or electroporation.

[0355] Engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes of the invention. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter may be induced by appropriate means (e.g., temperature shift or chemical induction) and the cells may be cultured for an additional period to allow them to produce the desired polypeptide or fragment thereof.

[0356] Cells can be harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract is retained for further purification. Microbial cells employed for expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents. Such methods are well known to those skilled in the art. The expressed polypeptide or fragment

can be recovered and purified from recombinant cell cultures by methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Protein refolding steps can be used, as necessary, in completing configuration of the polypeptide. If desired, high performance liquid chromatography (HPLC) can be employed for final purification steps.

[0357] Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts and other cell lines capable of expressing proteins from a compatible vector, such as the C127, 3T3, CHO, HeLa and BHK cell lines.

[0358] The constructs in host cells can be used in a conventional manner to produce the gene product encoded by the recombinant sequence. Depending upon the host employed in a recombinant production procedure, the polypeptides produced by host cells containing the vector may be glycosylated or may be non-glycosylated. Polypeptides of the invention may or may not also include an initial methionine amino acid residue.

[0359] Cell-free translation systems can also be employed to produce a polypeptide of the invention. Cell-free translation systems can use mRNAs transcribed from a DNA construct comprising a promoter operably linked to a nucleic acid encoding the polypeptide or fragment thereof. In some aspects, the DNA construct may be linearized prior to conducting an *in vitro* transcription reaction. The transcribed mRNA is then incubated with an appropriate cell-free translation extract, such as a rabbit reticulocyte extract, to produce the desired polypeptide or fragment thereof.

[0360] The expression vectors can contain one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells such as dihydrofolate reductase or neomycin resistance for eukaryotic cell culture, or such as tetracycline or ampicillin resistance in *E. coli*.

[0361] For transient expression in mammalian cells, cDNA encoding a polypeptide of interest may be incorporated into a mammalian expression vector, e.g. pcDNA1, which is available commercially from Invitrogen Corporation (San Diego, Calif., U.S.A.; catalogue

number V490-20). This is a multifunctional 4.2 kb plasmid vector designed for cDNA expression in eukaryotic systems, and cDNA analysis in prokaryotes, incorporated on the vector are the CMV promoter and enhancer, splice segment and polyadenylation signal, an SV40 and Polyoma virus origin of replication, and M13 origin to rescue single strand DNA for sequencing and mutagenesis, Sp6 and T7 RNA promoters for the production of sense and anti-sense RNA transcripts and a Col E1-like high copy plasmid origin. A polylinker is located appropriately downstream of the CMV promoter (and 3' of the T7 promoter).

[0362] The cDNA insert may be first released from the above phagemid incorporated at appropriate restriction sites in the pcDNAI polylinker. Sequencing across the junctions may be performed to confirm proper insert orientation in pcDNAI. The resulting plasmid may then be introduced for transient expression into a selected mammalian cell host, for example, the monkey-derived, fibroblast like cells of the COS-1 lineage (available from the American Type Culture Collection, Rockville, Md. as ATCC CRL 1650).

[0363] For transient expression of the protein-encoding DNA, for example, COS-1 cells may be transfected with approximately 8 μg DNA per 10^6 COS cells, by DEAE-mediated DNA transfection and treated with chloroquine according to the procedures described by Sambrook et al, Molecular Cloning: A Laboratory Manual, 1989, Cold Spring Harbor Laboratory Press, Cold Spring Harbor N.Y, pp. 16.30-16.37. An exemplary method is as follows. Briefly, COS-1 cells are plated at a density of 5 x 10^6 cells/dish and then grown for 24 hours in FBS-supplemented DMEM/F12 medium. Medium is then removed and cells are washed in PBS and then in medium. A transfection solution containing DEAE dextran (0.4 mg/ml), 100 μM chloroquine, 10% NuSerum, DNA (0.4 mg/ml) in DMEM/F12 medium is then applied on the cells 10 ml volume. After incubation for 3 hours at 37 °C, cells are washed in PBS and medium as just described and then shocked for 1 minute with 10% DMSO in DMEM/F12 medium. Cells are allowed to grow for 2-3 days in 10% FBS-supplemented medium, and at the end of incubation dishes are placed on ice, washed with ice cold PBS and then removed by scraping. Cells are then harvested by centrifugation at 1000 rpm for 10 minutes and the cellular pellet is frozen in liquid nitrogen, for subsequent use in protein expression. Northern blot analysis of a thawed aliquot of frozen cells may be used to confirm expression of receptor-encoding cDNA in cells under storage.

[0364] In a like manner, stably transfected cell lines can also prepared, for example, using two different cell types as host: CHO K1 and CHO Pro5. To construct these cell lines, cDNA coding for the relevant protein may be incorporated into the mammalian expression vector pRC/CMV (Invitrogen), which enables stable expression. Insertion at this site places the cDNA under the expression control of the cytomegalovirus promoter and upstream of the polyadenylation site and terminator of the bovine growth hormone gene, and into a vector background comprising the neomycin resistance gene (driven by the SV40 early promoter) as selectable marker.

[0365] An exemplary protocol to introduce plasmids constructed as described above is as follows. The host CHO cells are first seeded at a density of $5x10^5$ in 10% FBS-supplemented MEM medium. After growth for 24 hours, fresh medium is added to the plates and three hours later, the cells are transfected using the calcium phosphate-DNA co-precipitation procedure (Sambrook et al, supra). Briefly, 3 μg of DNA is mixed and incubated with buffered calcium solution for 10 minutes at room temperature. An equal volume of buffered phosphate solution is added and the suspension is incubated for 15 minutes at room temperature. Next, the incubated suspension is applied to the cells for 4 hours, removed and cells were shocked with medium containing 15% glycerol. Three minutes later, cells are washed with medium and incubated for 24 hours at normal growth conditions. Cells resistant to neomycin are selected in 10% FBS-supplemented alpha-MEM medium containing G418 (1 mg/ml). Individual colonies of G418-resistant cells are isolated about 2-3 weeks later, clonally selected and then propagated for assay purposes.

EXAMPLES

A number of examples involved in the present invention are described below. In most cases, alternative techniques could also be used. For example, techniques, methods, and other information described in U.S. Patent 5,837,815; U.S. Patent 5,837,524; U.S. Patent Publication 2002/0048782; PCT/US98/02797, WO 98/35056; and McShan *et al.*, *Internat. J. Oncology* 21:197-205 (2002) can be used in the present invention. Such techniques and information include, without limitation, cloning, culturing, purification, assaying, screening, use of modulators, sequence information, and information concerning biological role of PYK2. Each of these references is incorporated by reference herein in

its entirety, including drawings.

EXAMPLE 1: Cloning of PYK2 Kinase Domain

[0366] Kinase domain of PYK2 (amino acids 420 - 691) was amplified by polymerase chain reaction (PCR) using the specific primers 5'-TCCACAGCATATGATTGCCCGTGAAGA TGTGGT-3' (SEQ ID NO: 5) and 5'-CTCTCGTCGACCTACATGGCAATGTCCTTCTCCA-3' (SEQ ID NO: 6). The resulting PCR fragment was digested with *Nde*I and *Sal*I and was ligated into a modified pET15b vector (Novagen) with a cleavable N-terminal hexa-histidine tag (designated pET1S). PYK2 coding sequence has been deposited with GenBank under accession number U33284. A desired PYK2 sequence can be obtained using PCR with a brain (*e.g.*, human brain) cDNA library, such as obtaining kinase domain using the above primers in PCR. The multi-cloning site of the pET15S vector is shown in the following sequence (SEQ ID NO: 7), including the sequence encoding the N-terminal hexa-histadine tag:

T7 promoter

AGATCTCGATCCCGCGAAATTAATACGACTCACTATAGGGGAATTGTGAGCGGATAACAATTCCCC

RBS

TCTAGAAATAATTTTGTTTAACTTTAAGAAGGAGATATACC

NdeI

ATGGGCAGCAGCCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGC**CATATG**GGATCCGG

M G S S H H H H H H S S G L V P R G S H M --------

StuI **SalI**

AATTCAAAGGCCTAC**GTCGAC**TAGAGCCTGCAGT*CTCGAC*CATCATCATCATCATCATTAATAAAAGG[redacted]

---------- *

SpeI **BamHI**

[redacted]GGCCGTT**ACTAGT**GGATCCGGCTGCTAACAAAGCCCGAAAGGAAGCTGAGTTGG

IVEX-3 Primer

Bpu1102 I **T7 terminator**

CTGCTGCCACC[redacted]ACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTG

3'-PET Primer

[0367] pET15S vector is derived from pET15b vector (Novagen) for bacterial expression to produce the proteins with N-terminal His6. This vector was modified by

replacement of NdeI-BamHI fragment to others to create SalI site and stop codon (TAG). Vector size is 5814 bp. Insert can be put using NdeI-SalI site.

[0368]

[0369] The amino acid and nucleic acid sequences for the PYK2 kinase domain utilized are provided in Table 4 (SEQ ID NO: 1 and 3 respectively).

EXAMPLE 2: Expression and Purification of PYK2 Kinase Domain

[0370] For protein expression Pyk2 kinase domain was transformed into *E. coli* strain BL21 (DE3) pLysS and transformants were selected on LB plates containing Kanamycin. Single colonies were grown overnight at 37°C in 200ml TB (terrific broth) media. 16x1L of fresh TB media in 2.8L flasks were inoculated with 10ml of overnight culture and grown with constant shaking at 37°C. Once cultures reached an absorbance of 1.0 at 600nm, 1mM isopropyl-β-D-thiogalactopyranoside (IPTG) was added and cultures were allowed to grow for a further 12hrs at 22°C with constant shaking. Cells were harvested by centrifugation at 7000 x g and pellets were frozen in liquid nitrogen and stored at –80°C until ready for lysis.

[0371] The cell pellet was suspended in lysis buffer containing 0.1M Potassium phosphate buffer pH 8.0, 200mM NaCl, 10%Glycerol, 2mm PMSF and EDTA free protease inhibitor cocktail tablets (Roche). Cells were lysed using a microfuidizer processor (Microfuidics Corporation) and insoluble cellular debris was removed using centrifugation at 30,000 x g. The cleared supernatant was added to Talon resin (Clonetech) and incubated for 4hrs at 4°C with constant rocking. The suspension was loaded onto a column and washed with 20 column volumes of lysis buffer plus 10mM Imadazole. Protein was eluted step wise with addition of lysis buffer plus 200mM Imadazole pH7.5 and 1ml fractions collected. Fractions containing PYK2 were pooled, concentrated and loaded onto a Pharmacia HiLoad 26/60 Superdex 200 sizing column (Pharmacia) pre-equilibrated with 20mM Tris pH7.5, 150mM NaCl.

[0372] Peak fractions were collected and assayed by SDS-PAGE. Fractions containing PYK2 were pooled and diluted in Tris buffer pH 7.5, until 30mM NaCl was reached. Diluted protein was further subjected to anion exchange chromatography using a Source

15Q (Pharmacia) sepharose column equilibrated with 20mM Tris pH7.5. Elution was performed using a linear gradient of sodium chloride (0-500mM). Eluted protein was treated with 2U thrombin per mg protein to remove N-terminal Histidine tag. Following cleavage Pyk2 was re-applied to Source 15Q (Pharmacia) sepharose column equilibrated with 20mM Tris pH7.5, and eluted using a linear sodium chloride gradient. Purified protein was concentrated to 100mg/ml and stored at –80°C until ready for crystallization screening.

Example 3: Crystallization of PYK2 Kinase Domain

[0373] Crystallization conditions were initially identified in the Hampton Research (Riverside, CA) screening kit (1). Optimized crystals were grown by vapor diffusion in sitting drop plates with equal volumes of protein solution of 10 mg/ml containing 20mM Tris-HCl pH 8.0, 150mM NaCl, 14mM BME, 1mM DTT and reservoir solution containing 8% polyethylene glycol (PEG) 8000, 0.2M Sodium Acetate, 0.1M Cacodylate pH 6.5, 20% Glycerol). Blades of crystals grew overnight at 4°C. Microseeding was used to produce larger, single crystals, the largest crystal being around 0.3mm X 0.05mm X 0.02mm.

Example 4: Diffraction Analysis of PYK2

[0374] Synchrotron X-ray data for Pyk2 was collected at beamline 8.3.1 of the Advanced Light Source (ALS, Lawrence Berkeley National Laboratory, Berkeley) on a Quantum 210 charge-coupled device detector (λ = 1.10Å). The mother liquor from the reservoir was used as cryo-protectant for the crystal. Detector distance was 110mm and exposure time was 10s per frame. 200 frames were collected with 0.5° oscillation over a wedge of 100°. The quality and resolution limits of the diffraction pattern were considerably improved by annealing the crystal. The crystal was briefly allowed to warm up for 10 seconds by shutting off the Nitrogen cryo stream and refrozen by resuming cooling with the cryo stream. Crystals of PYK2 diffracted to a resolution limit of 1.45 Å with cell dimensions of a = 37Å, b = 47Å, c = 81Å, α = 90°, β = 92°, γ = 90°. The data were processed using Mosflm () and scaled and reduced with Scala () in CCP4 () in space group P2. The data processing process was driven by the ELVES automation scripts (J. M. Holton, unpublished data). An inspection of the 0K0 zone indicated that all odd (2n+1)

reflections were very weak compared with the even reflections, suggesting the space group to be $P2_1$.

PYK2 Structure Determination and Refinement

[0375] The initial phases for the dataset were obtained by molecular replacement. A homology model of the protein Pyk2 was generated using the LCK kinase structure (PDBID: 1qpc) as a template. This model was trimmed by excising all loops before being used in molecular replacement program EPMR (), which resulted in a solution with CC=0.372. The molecular replacement solution phases were improved by the program Arp-Warp (). The resultant model was further improved by manual model building and extension in O () and refinement with CNX () and Refmac5 () in CCP4. The cycle of model building and refinement continued till the model was complete and refinement converged to the R/Rfree of 20.83/26.94 %. The geometric analysis of the model was performed by PROCHECK () which indicated the structure to have excellent geometry.

[0376] Data collection and refinement statistics for PYK2 kinase domain crystal, and for PYK2 kinase domain/binding compound cocrystal are summarized in the following table:

Data Collection and Refinement Statistics

	Pyk2 (APO)	**Pyk2+AMPPNP**
Crystal Parameters		
Space Group	$P2_1$	$P2_1$
Unit Cell (Å)	a=37.17, b=46.97, c=80.36, □=92.63	a=37.32, b=46.98, c=81.11, □=92.83
Number of molecules/AU	1	1
V_M ($Å^3$/Dalton)	2.4	2.4
Solvent content (%)	48	48
Data Collection and Processing		
Resolution (Å)	1.45	1.80
Wavelength (Å)	1.1	1.1
Unique reflections	47843	26149

Redundancy (last shell*)	2.0 (1.8)	4.0 (2.9)
Completeness (last shell) (%)	97.5 (88.9)	99.8 (97.8)
I/□ (last shell)	10.9 (1.3)	12.0 (2.3)
R_{sym} (last shell)	0.043 (0.487)	0.063 (0.459)
*Last shell (Å)	1.49 – 1.45	1.85 – 1.80
Refinement		
R_{work} / R_{free} (%)	16.93/20.68	18.62/22.81
Number of Atoms	2583	2507
Rmsd from ideal geometry	0.012 (bond distance), 1.434 (bond angle)	0.010 (bond distance), 1.372 (bond angle)
SigmaA coordinate error	0.16 Å (for 5.0-1.45 Å)	0.14 Å (for 5.0-1.80 Å)
Average B-factors (Å^2)	19.3	20.5
Protein atoms	16.4	19.0
Waters	37.6	34.3
Ligand	-	44.41

[0377] The model of Pyk2 contains 273 amino acids (spanning the PYK2 sequence 420-691 with one residue from the cloning vector) and 180 water molecules. The Pyk2 structure adopts the standard kinase fold consisting of an N-terminal β-sheet domain and a C-terminal α-helical domain linked by a 5 residue linker. The linker segment contains the canonical H-bond acceptor/donor residues E503 and Y505 that would normally interact with the adenosine ring of ATP. In the apo structure these residues make H-bonds with water molecules.

[0378] A ribbon diagram of the PYK2 active site is shown in Figure 1. Atomic coordinates for the apo protein are provided in Table 1, while atomic coordinates for a PYK2 co-crystallized with a binding compound (AMPPNP) are provided in Table 2.

Active Loop Conformation

[0379] In many protein kinases, the activation loop, or A-loop, plays an important role in regulating the kinase activity. In active kinases, the A-loops adopt a highly similar

conformation characterized by the formation of three small β-sheet moieties: two with the main body of the protein (the beginning of the catalytic or C-loop and the αEF/αF loop, respectively), and one with the substrate peptide. In contrast, the inactive conformation of A-loop differs markedly from protein to protein, albeit having the similar effect of blocking ATP binding, substrate-binding, or both. In comparison with the active insulin receptor (INSR) and IGFR1 kinase domain strutures, the A-loop in the solved Pyk2 structure is clearly in an inactive conformation. The loop is stabilized by a unique set of intra- and inter-loop interactions that differentiate it from all known A-loop structures.

[0380] The A-loop in our Pyk2 structure starts to deviate from the standard active conformation at the DFG motif (for comparison, we modeled the active A-loop conformation of Pyk2 based on the IGFR1 structure). The first two residues of the DFG motif (D^{567} and F^{568}) have similar orientations as their counterparts in the active A-loop form, with D^{567} interacting with K^{457} (β3) and F^{568} locked in a hydrophobic pocket sandwiched by two residues (I^{477} and M^{478}) from αC. However, the third residue in the motif, G^{569}, adopts a completely different conformation, resulting in the formation of a hydrogen bond beween G^{567}:NH and H^{547}:CO. This hydrogen bond forces the A-loop to a different path that precludes it from forming a β-sheet with C-loop. A similar hydrogen bond has also been observed in two other tyrosine kinases: HCK (1qcf) and SRC (1fmk).

[0381] There are multiple interactions that help to stabilize the A-loop in its observed conformation. Most of them involve a unique sequence moiety of Pyk2. Among the tyrosine kinases of known structure, Pyk2 contains a unique ED repeat (E^{575}-D^{578}) in the A-loop. In the Pyk2 structure, E^{575} is exposed to solvent, whereas D^{576} initiates a tight β-turn. Beside providing the canonical β-turn backbone hydrogen bond between D^{576}:CO-Y^{579}:NH, the side chain of D^{576} also interacts with D^{578}:NH. The β-turn region of A-loop is held to the αEF/αF loop by two side-chain–backbone hydrogen bonds: one between E^{577}:CO-R^{600}:N^{ϵ} and the other between K^{581}:NZ-N^{598}:CO. The side chain of E^{577} interacts with the end of the activation loop via two hydrogen bonds, one with T^{585} (OG) and the other with R^{586} (NH). The most interesting feature of the Pyk2 A-loop is the salt bridge formed between D^{588} and R^{547} from the C-loop (the distances between the two OD and two NH atoms are 2.9A). Neither of the two tyrosines Y^{579} and Y^{580} is phosphorylated in our structure. Y^{579} is exposed to solvent, whereas Y^{580} binds to the hydrophobic portions of the E^{575} and E^{577} side chains.

[0382] Because FAK does not have the second ED, the conformation of the A-loop in an inactive FAK is expected to be different.

Implications for substrate binding and autophosphorylation

[0383] An important event in the enzymatic activation of FAK/Pyk2 is the autophosphorylation of a tyrosine residue before the catalytic domain (Y402). The phosphorylated Y402 provides the binding site for Src and other related kinases and facilitates Src-dependent phosphorylation of other tyrosine residues on Pyk2 including Y579 and Y580. It is not clear how autophosphorylation could occur before Y579 and Y580 are phosphorylated.

[0384] To test whether Y402 can reach the substrate binding site, we modeled the 7 residue peptide D^{400}IYAEIPD^{407} containing Y^{402} into the substrate binding site based on the cocrystal structure of IGFR1 kinase domain with its substrate peptide. In our protein construct, the Pyk2 insert starts at I420. There are four residues (GSHM) N-terminal to I420 left by the His-tag used, of those only M419 is visible. We then modeled the 11 residues that link D419 to M407. The model shows that, in order to reach the substrate binding site, the N-terminal region has to transverse along the back of αC. The link would also fix the A-loop in the active conformation. This may provide the mechanism that the protein used to autophosphorylate Y402. Once Y402 is phosphorylated, the N-terminus is then released and subject to SH2 binding. The A-loop also becomes flexible and accessible to Src.

[0385] Because the residues surrounding the P+1 and P+3 binding pocket are mostly hydrophobic in tyrosine kinases, substrate P+1 and P+3 sites are mostly hydrophobic residues. The residue that might interact with P+2 varies. Acidic and other polar site chains might be preferred because of the nearby residue R586. The P-1 site is an acidic residue in INSR and IGFR1. The residue for interacting with P-1 is Arg; this residue is changed to Gly in Pyk2, leaving the space largely hydrophobic. The autophosphorylation site sequence in Pyk2, IYAEIPD, and the sequences of several other known Pyk2 phosphorylation sites fit well the substrate selectivity profile of Pyk2.

Example 5: PYK2 Binding Assays

[0386] Binding assays can be performed in a variety of ways, including a variety of ways known in the art. For example, competitive binding to PYK2 can be measured on Nickel-FlashPlates, using His-tagged PYK2 (~ 100 ng) and ATPγ[^{35}S] (~ 10 nCi). As compound is added, the signal decreases, since less ATPγ[^{35}S] is bound to PYK2 which is proximal to the scintillant in the FlashPlate. The binding assay can be performed by the addition of compound (10 μl; 20 mM) to PYK2 protein or kinase domain (90 10 μl) followed by the addition of ATPγ[^{35}S] and incubating for 1 hr at 37°C. The radioactivity is measured through scintillation counting in Trilus (Perkin-Elmer).

[0387] Alternatively, any method which can measure binding of a ligand to the ATP-binding site can be used. For example, a fluorescent ligand can be used. When bound to PYK2, the emitted fluorescence is polarized. Once displaced by inhibitor binding, the polarization decreases.

[0388] Determination of IC50 for compounds by competitive binding assays. (Note that K_I is the dissociation constant for inhibitor binding; K_D is the dissociation constant for substrate binding.) For this system, the IC50, inhibitor binding constant and substrate binding constant can be interrelated according to the following formula:

[0389] When using radiolabeled substrate $K_I = \frac{IC50}{1 + [L^*]/K_D}$,

[0390] the IC50 ~ K_I when there is a small amount of labeled substrate.

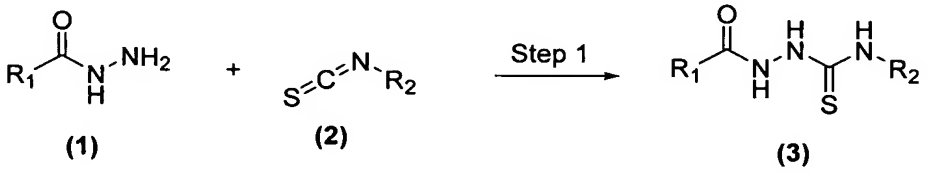
Example 6: PYK2 Activity Assay

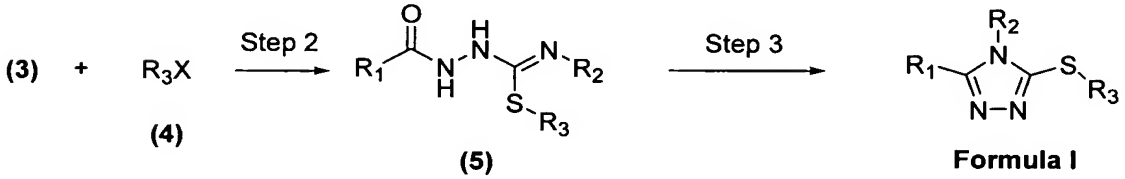
[0391] As an exemplary kinase assay, the kinase activity of PYK2 was measured in AlphaScreening (Packard BioScience). The kinase buffer (HMNB) contains HEPES 50mM at pH7.2, Mg/Mn 5mM each, NP-40 0.1%, and BSA at final 50ug/ml. AlphaScreening is conducted as described by the manufacturer. In brief, the kinase reaction is performed in 384-well plate in 25ul volume. The substrate is biotin-$(E4Y)_3$ at final concentration of 1nM. The final concentration of ATP is 10uM. For compound testing the final DMSO concentration is 1%. The reaction is incubated in 31°C for 1 hour.

[0392] The Pyk2 kinase domain residues 419 to 691 is an active kinase in AlphaScreen. At a concentration of 8ng/well in 384-well plate, PYK2 shows a Kd of 7.34uM, which is in general agreement with most protein kinases (Table 5). Inhibition by ATP analogs was tested with Pyk2 at 8ng/well and ATP at 10uM. The data is shown in Table 5. The affinity of ATP-g-S and ADP with Pyk2 is at 14uM. Adenosine and AMP-PCP have little effect on PYK2 in the concentration tested.

Example 9: Synthesis of the Compounds of Formula I:

Scheme -1





[0393] The triazole derivatives, represented by Formula I, can be prepared as shown in Scheme-1.

Step-1 Preparation of formula (3)

[0394] The compound of formula (3) is prepared conventionally by reaction of a compound of formula (1), where R_1 = alkyl, aryl, heteroaryl (e.g. *m*-toluic hydrazide), with an isothiocyanate of formula (2), in a basic solvent (e.g. pyridine), typically heated near 65 °C for 2-6 hours.

Step-2 Preparation of formula (5)

[0395] The compound of formula (5) is prepared conventionally by reaction of a compound of formula (3) with an alkylating agent of formula (4)(e.g. methyl iodide), in an inert solvent (e.g. THF) at room temperature for 24 -48 hours.

Step-3 Preparation of Formula I

[0396] The compound of Formula I is prepared by dissolving a compound of formula (5) in POCl3 and heated near 80 °C for 8 -12 hours. When the reaction is substantially complete, the product of Formula I is isolated by conventional means (e.g. reverse phase HPLC). Smith, et. al., *J. Comb. Chem.*, **1999**, *1*, 368-370; and references therein.

Example 10: Site-directed Mutagenesis of PYK2 kinase

[0397] Mutagenesis of PYK2 kinase can be carried out according to the following procedure as described in Molecular Biology: Current Innovations and Future Trends. Eds. A.M. Griffin and H.G.Griffin. (1995) ISBN 1-898486-01-8, Horizon Scientific Press, PO Box 1, Wymondham, Norfolk, U.K., among others.

[0398] In vitro site-directed mutagenesis is an invaluable technique for studying protein structure-function relationships, gene expression and vector modification. Several methods have appeared in the literature, but many of these methods require single-stranded DNA as the template. The reason for this, historically, has been the need for separating the complementary strands to prevent reannealing. Use of PCR in site-directed mutagenesis accomplishes strand separation by using a denaturing step to separate the complementing strands and allowing efficient polymerization of the PCR primers. PCR site-directed methods thus allow site-specific mutations to be incorporated in virtually any double-stranded plasmid; eliminating the need for M13-based vectors or single-stranded rescue.

[0399] It is often desirable to reduce the number of cycles during PCR when performing PCR-based site-directed mutagenesis to prevent clonal expansion of any (undesired) second-site mutations. Limited cycling which would result in reduced product yield, is offset by increasing the starting template concentration. A selection is used to reduce the number of parental molecules coming through the reaction. Also, in order to use a single PCR primer set, it is desirable to optimize the long PCR method. Further, because of the extendase activity of some thermostable polymerases it is often necessary to incorporate

an end-polishing step into the procedure prior to end-to-end ligation of the PCR-generated product containing the incorporated mutations in one or both PCR primers.

[0400] The following protocol provides a facile method for site-directed mutagenesis and accomplishes the above desired features by the incorporation of the following steps: (i) increasing template concentration approximately 1000-fold over conventional PCR conditions; (ii) reducing the number of cycles from 25-30 to 5-10; (iii) adding the restriction endonuclease DpnI (recognition target sequence: 5-Gm6ATC-3, where the A residue is methylated) to select against parental DNA (note: DNA isolated from almost all common strains of E. coli is Dam-methylated at the sequence 5-GATC-3); (iv) using Taq Extender in the PCR mix for increased reliability for PCR to 10 kb; (v) using Pfu DNA polymerase to polish the ends of the PCR product, and (vi) efficient intramolecular ligation in the presence of T4 DNA ligase.

[0401] Plasmid template DNA (approximately 0.5 pmole) is added to a PCR cocktail containing, in 25 ul of 1x mutagenesis buffer: (20 mM Tris HCl, pH 7.5; 8 mM MgCl2; 40 ug/ml BSA); 12-20 pmole of each primer (one of which must contain a 5-prime phosphate), 250 uM each dNTP, 2.5 U Taq DNA polymerase, 2.5 U of Taq Extender (Stratagene).

[0402] The PCR cycling parameters are 1 cycle of: 4 min at 94 C, 2 min at 50 C and 2 min at 72 C; followed by 5-10 cycles of 1 min at 94 C, 2 min at 54 C and 1 min at 72 C (step 1).

[0403] The parental template DNA and the linear, mutagenesis-primer incorporating newly synthesized DNA are treated with DpnI (10 U) and Pfu DNA polymerase (2.5U). This results in the DpnI digestion of the in vivo methylated parental template and hybrid DNA and the removal, by Pfu DNA polymerase, of the Taq DNA polymerase-extended base(s) on the linear PCR product.

[0404] The reaction is incubated at 37 C for 30 min and then transferred to 72 C for an additional 30 min (step 2).

[0405] Mutagenesis buffer (1x, 115 ul, containing 0.5 mM ATP) is added to the DpnI-digested, Pfu DNA polymerase-polished PCR products.

[0406] The solution is mixed and 10 ul is removed to a new microfuge tube and T4 DNA ligase (2-4 U) added.

[0407] The ligation is incubated for greater than 60 min at 37 C (step 3).

[0408] The treated solution is transformed into competent E. coli (step 4).

[0409] In addition to the PCT-based site-directed mutagenesis described above, other methods are available. Examples include those described in Kunkel (1985) Proc. Natl. Acad. Sci. 82:488-492; Eckstein et al. (1985) Nucl. Acids Res. 13:8764-8785; and using the GeneEditor™ Site-Directed Mutageneis Sytem from Promega.

[0410] All patents and other references cited in the specification are indicative of the level of skill of those skilled in the art to which the invention pertains, and are incorporated by reference in their entireties, including any tables and figures, to the same extent as if each reference had been incorporated by reference in its entirety individually.

[0411] One skilled in the art would readily appreciate that the present invention is well adapted to obtain the ends and advantages mentioned, as well as those inherent therein. The methods, variances, and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the invention, are defined by the scope of the claims.

[0412] It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. For example, variations can be made to crystallization or co-crystallization conditions for PYK2 proteins and/or various kinase domain sequences can be used. Thus, such additional embodiments are within the scope of the present invention and the following claims.

[0413] The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms

"comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

[0414] In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

[0415] Also, unless indicated to the contrary, where various numerical values are provided for embodiments, additional embodiments are described by taking any 2 different values as the endpoints of a range. Such ranges are also within the scope of the described invention.

[0416] Thus, additional embodiments are within the scope of the invention and within the following claims.

Table 1

```
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REMARK   3   PROGRAM     : REFMAC 5.1.25
REMARK   3   AUTHORS     : MURSHUDOV,VAGIN,DODSON
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REMARK   3  FIT TO DATA USED IN REFINEMENT.
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ATOM      8  CG  MET A 419     -19.078  14.098  24.049  1.00 39.47      A    C
ANISOU    8  CG  MET A 419     4983   5017   4994    -61    -50      8  A    C
ATOM     11  SD  MET A 419     -18.149  12.778  23.218  1.00 42.55      A    S
ANISOU   11  SD  MET A 419     5414   5343   5409     11     26    -34  A    S
ATOM     12  CE  MET A 419     -17.963  11.571  24.548  1.00 42.75      A    C
ANISOU   12  CE  MET A 419     5417   5401   5423    -17    -19     12  A    C
ATOM     16  C   MET A 419     -16.343  15.776  26.257  1.00 35.96      A    C
ANISOU   16  C   MET A 419     4538   4570   4553     -2     21      4  A    C
ATOM     17  O   MET A 419     -16.823  16.469  27.161  1.00 36.07      A    O
ANISOU   17  O   MET A 419     4561   4581   4561     -5     15    -19  A    O
ATOM     20  N   ILE A 420     -15.136  15.980  25.730  1.00 34.59      A    N
ANISOU   20  N   ILE A 420     4374   4378   4388      7    -11    -22  A    N
ATOM     22  CA  ILE A 420     -14.140  16.850  26.347  1.00 33.36      A    C
ANISOU   22  CA  ILE A 420     4229   4219   4225     20      2      7  A    C
ATOM     24  CB  ILE A 420     -12.741  16.141  26.376  1.00 33.70      A    C
ANISOU   24  CB  ILE A 420     4255   4286   4261     15      4    -12  A    C
ATOM     26  CG1 ILE A 420     -11.770  16.911  27.282  1.00 34.11      A    C
ANISOU   26  CG1 ILE A 420     4297   4329   4332     12    -13      0  A    C
ATOM     29  CD1 ILE A 420     -10.797  17.813  26.577  1.00 34.87      A    C
ANISOU   29  CD1 ILE A 420     4423   4406   4417     -5     13     28  A    C
ATOM     33  CG2 ILE A 420     -12.180  15.885  24.948  1.00 34.10      A    C
ANISOU   33  CG2 ILE A 420     4312   4331   4310      1     23      6  A    C
ATOM     37  C   ILE A 420     -14.057  18.233  25.694  1.00 31.72      A    C
ANISOU   37  C   ILE A 420     4002   4045   4003     25     -4    -28  A    C
ATOM     38  O   ILE A 420     -13.902  18.365  24.480  1.00 32.15      A    O
ANISOU   38  O   ILE A 420     4033   4132   4050     36    -20     13  A    O
ATOM     39  N   ALA A 421     -14.152  19.265  26.522  1.00 29.54      A    N
ANISOU   39  N   ALA A 421     3728   3740   3757     13    -21     49  A    N
ATOM     41  CA  ALA A 421     -14.110  20.642  26.055  1.00 27.85      A    C
ANISOU   41  CA  ALA A 421     3497   3550   3531    -15    -12      6  A    C
ATOM     43  CB  ALA A 421     -15.025  21.514  26.899  1.00 27.73      A    C
ANISOU   43  CB  ALA A 421     3508   3516   3512      2     -4     23  A    C
ATOM     47  C   ALA A 421     -12.683  21.138  26.141  1.00 26.04      A    C
ANISOU   47  C   ALA A 421     3309   3286   3297     18      0     47  A    C
ATOM     48  O   ALA A 421     -11.905  20.642  26.948  1.00 25.36      A    O
ANISOU   48  O   ALA A 421     3159   3228   3247     37     -3      6  A    O
ATOM     49  N   ARG A 422     -12.355  22.138  25.331  1.00 24.01      A    N
ANISOU   49  N   ARG A 422     2992   3084   3046     16     -1     27  A    N
ATOM     51  CA  ARG A 422     -11.041  22.756  25.366  1.00 22.30      A    C
ANISOU   51  CA  ARG A 422     2845   2819   2806     27      3     27  A    C
ATOM     53  CB  ARG A 422     -10.917  23.847  24.290  1.00 21.96      A    C
ANISOU   53  CB  ARG A 422     2771   2807   2766     36     -4     32  A    C
ATOM     56  CG  ARG A 422      -9.490  24.349  24.085  1.00 21.12      A    C
ANISOU   56  CG  ARG A 422     2765   2618   2642     -5      1     39  A    C
ATOM     59  CD  ARG A 422      -9.378  25.523  23.138  1.00 19.52      A    C
ANISOU   59  CD  ARG A 422     2505   2472   2436     15    -28    -27  A    C
ATOM     62  NE  ARG A 422      -9.899  25.202  21.812  1.00 18.34      A    N
ANISOU   62  NE  ARG A 422     2363   2273   2332     80    -13     23  A    N
ATOM     64  CZ  ARG A 422      -9.213  24.608  20.840  1.00 16.29      A    C
ANISOU   64  CZ  ARG A 422     2110   2022   2056    -41    -63      7  A    C
ATOM     65  NH1 ARG A 422      -7.965  24.214  21.025  1.00 14.80      A    N
ANISOU   65  NH1 ARG A 422     2022   1925   1676    -41     -5    -25  A    N
ATOM     68  NH2 ARG A 422      -9.790  24.379  19.671  1.00 16.03      A    N
ANISOU   68  NH2 ARG A 422     2044   2056   1991     55   -106    122  A    N
ATOM     71  C   ARG A 422     -10.711  23.323  26.738  1.00 21.24      A    C
ANISOU   71  C   ARG A 422     2688   2703   2677     31     27     34  A    C
ATOM     72  O   ARG A 422      -9.578  23.209  27.188  1.00 20.08      A    O
ANISOU   72  O   ARG A 422     2563   2589   2475     42     80     71  A    O
ATOM     73  N   GLU A 423     -11.706  23.897  27.411  1.00 20.34      A    N
ANISOU   73  N   GLU A 423     2580   2572   2576     57     -1     48  A    N
ATOM     75  CA  GLU A 423     -11.503  24.533  28.707  1.00 20.07      A    C
ANISOU   75  CA  GLU A 423     2550   2531   2542     52      1     38  A    C
ATOM     77  CB  GLU A 423     -12.724  25.406  29.090  1.00 20.68      A    C
ANISOU   77  CB  GLU A 423     2584   2640   2634     71     35     31  A    C
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ATOM	80	CG	GLU	A	423	-12.476	26.414	30.216	1.00	23.54		A	C
ANISOU	80	CG	GLU	A	423	3027	3008	2907	-79	-35	-10	A	C
ATOM	83	CD	GLU	A	423	-13.574	27.477	30.362	1.00	26.82		A	C
ANISOU	83	CD	GLU	A	423	3409	3383	3395	45	-9	1	A	C
ATOM	84	OE1	GLU	A	423	-14.777	27.122	30.416	1.00	29.98		A	O
ANISOU	84	OE1	GLU	A	423	3624	3986	3778	-102	18	77	A	O
ATOM	85	OE2	GLU	A	423	-13.251	28.688	30.433	1.00	27.61		A	O
ANISOU	85	OE2	GLU	A	423	3581	3449	3461	-64	-77	-21	A	O
ATOM	86	C	GLU	A	423	-11.209	23.499	29.810	1.00	18.81		A	C
ANISOU	86	C	GLU	A	423	2381	2373	2390	43	19	20	A	C
ATOM	87	O	GLU	A	423	-10.737	23.875	30.866	1.00	18.11		A	O
ANISOU	87	O	GLU	A	423	2335	2198	2347	163	39	1	A	O
ATOM	88	N	ASP	A	424	-11.483	22.214	29.555	1.00	17.37		A	N
ANISOU	88	N	ASP	A	424	2170	2251	2179	93	40	40	A	N
ATOM	90	CA	ASP	A	424	-11.106	21.134	30.486	1.00	16.78		A	C
ANISOU	90	CA	ASP	A	424	2076	2178	2122	63	62	33	A	C
ATOM	92	CB	ASP	A	424	-11.801	19.810	30.126	1.00	16.79		A	C
ANISOU	92	CB	ASP	A	424	2124	2186	2066	65	15	51	A	C
ATOM	95	CG	ASP	A	424	-13.310	19.872	30.235	1.00	18.67		A	C
ANISOU	95	CG	ASP	A	424	2322	2411	2361	-32	25	88	A	C
ATOM	96	OD1	ASP	A	424	-13.822	20.689	31.012	1.00	20.52		A	O
ANISOU	96	OD1	ASP	A	424	2501	2731	2565	98	55	2	A	O
ATOM	97	OD2	ASP	A	424	-14.059	19.117	29.590	1.00	20.81		A	O
ANISOU	97	OD2	ASP	A	424	2670	2802	2434	-141	-145	110	A	O
ATOM	98	C	ASP	A	424	-9.591	20.887	30.510	1.00	16.59		A	C
ANISOU	98	C	ASP	A	424	2045	2175	2084	58	19	79	A	C
ATOM	99	O	ASP	A	424	-9.095	20.193	31.394	1.00	15.30		A	O
ANISOU	99	O	ASP	A	424	1760	2109	1944	95	117	137	A	O
ATOM	100	N	VAL	A	425	-8.866	21.439	29.537	1.00	15.79		A	N
ANISOU	100	N	VAL	A	425	1968	2034	1998	81	36	53	A	N
ATOM	102	CA	VAL	A	425	-7.433	21.180	29.400	1.00	16.53		A	C
ANISOU	102	CA	VAL	A	425	2060	2116	2104	36	6	47	A	C
ATOM	104	CB	VAL	A	425	-7.084	20.492	28.062	1.00	16.10		A	C
ANISOU	104	CB	VAL	A	425	2052	2052	2014	63	6	94	A	C
ATOM	106	CG1	VAL	A	425	-5.577	20.299	27.943	1.00	17.51		A	C
ANISOU	106	CG1	VAL	A	425	2169	2241	2244	19	40	56	A	C
ATOM	110	CG2	VAL	A	425	-7.780	19.162	27.934	1.00	16.93		A	C
ANISOU	110	CG2	VAL	A	425	2140	2180	2111	13	45	-29	A	C
ATOM	114	C	VAL	A	425	-6.715	22.499	29.464	1.00	16.70		A	C
ANISOU	114	C	VAL	A	425	2095	2109	2141	35	21	39	A	C
ATOM	115	O	VAL	A	425	-7.006	23.392	28.650	1.00	17.77		A	O
ANISOU	115	O	VAL	A	425	2229	2267	2253	-18	-21	164	A	O
ATOM	116	N	VAL	A	426	-5.821	22.635	30.442	1.00	16.43		A	N
ANISOU	116	N	VAL	A	426	2046	2074	2121	62	-2	56	A	N
ATOM	118	CA	VAL	A	426	-4.993	23.823	30.616	1.00	16.84		A	C
ANISOU	118	CA	VAL	A	426	2106	2097	2194	49	16	37	A	C
ATOM	120	CB	VAL	A	426	-5.078	24.352	32.052	1.00	17.23		A	C
ANISOU	120	CB	VAL	A	426	2147	2187	2210	20	-4	53	A	C
ATOM	122	CG1	VAL	A	426	-4.207	25.586	32.233	1.00	18.25		A	C
ANISOU	122	CG1	VAL	A	426	2299	2325	2309	-30	3	0	A	C
ATOM	126	CG2	VAL	A	426	-6.534	24.674	32.402	1.00	17.11		A	C
ANISOU	126	CG2	VAL	A	426	2153	2093	2254	48	24	25	A	C
ATOM	130	C	VAL	A	426	-3.534	23.506	30.292	1.00	16.82		A	C
ANISOU	130	C	VAL	A	426	2114	2104	2170	38	43	46	A	C
ATOM	131	O	VAL	A	426	-2.935	22.615	30.889	1.00	17.14		A	O
ANISOU	131	O	VAL	A	426	2107	2165	2237	41	32	125	A	O
ATOM	132	N	LEU	A	427	-2.973	24.235	29.340	1.00	16.42		A	N
ANISOU	132	N	LEU	A	427	2112	1992	2133	31	37	13	A	N
ATOM	134	CA	LEU	A	427	-1.595	24.028	28.926	1.00	16.16		A	C
ANISOU	134	CA	LEU	A	427	2057	1994	2087	-4	13	-1	A	C
ATOM	136	CB	LEU	A	427	-1.409	24.452	27.473	1.00	15.99		A	C
ANISOU	136	CB	LEU	A	427	2026	2006	2044	-10	-4	0	A	C
ATOM	139	CG	LEU	A	427	-2.397	23.859	26.453	1.00	15.54		A	C
ANISOU	139	CG	LEU	A	427	1898	2022	1982	-24	16	22	A	C
ATOM	141	CD1	LEU	A	427	-2.113	24.393	25.052	1.00	15.79		A	C
ANISOU	141	CD1	LEU	A	427	1866	2116	2017	-36	35	23	A	C
ATOM	145	CD2	LEU	A	427	-2.417	22.333	26.481	1.00	15.07		A	C

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ANISOU  145  CD2 LEU A 427     1790   2024   1911    -15     57     33  A    C
ATOM    149  C   LEU A 427      -0.667  24.823  29.826  1.00 16.42           A    C
ANISOU  149  C   LEU A 427     2122   2010   2105    -15     11    -28  A    C
ATOM    150  O   LEU A 427      -0.931  25.985  30.099  1.00 16.32           A    O
ANISOU  150  O   LEU A 427     2169   1842   2188     15     15     18  A    O
ATOM    151  N   ASN A 428       0.417  24.199  30.284  1.00 16.65           A    N
ANISOU  151  N   ASN A 428     2139   2031   2154     -4     -2    -29  A    N
ATOM    153  CA  ASN A 428       1.375  24.848  31.192  1.00 17.77           A    C
ANISOU  153  CA  ASN A 428     2266   2207   2279    -14    -32    -45  A    C
ATOM    155  CB  ASN A 428       1.598  23.981  32.430  1.00 18.50           A    C
ANISOU  155  CB  ASN A 428     2377   2344   2306    -40    -65    -41  A    C
ATOM    158  CG  ASN A 428       0.304  23.646  33.156  1.00 20.68           A    C
ANISOU  158  CG  ASN A 428     2577   2704   2574    -19    -10    -38  A    C
ATOM    159  OD1 ASN A 428       0.066  22.488  33.532  1.00 24.63           A    O
ANISOU  159  OD1 ASN A 428     3195   3072   3091   -115    -67    140  A    O
ATOM    160  ND2 ASN A 428      -0.544  24.648  33.345  1.00 23.16           A    N
ANISOU  160  ND2 ASN A 428     2906   2948   2943     70     29     -1  A    N
ATOM    163  C   ASN A 428       2.731  25.180  30.562  1.00 18.24           A    C
ANISOU  163  C   ASN A 428     2302   2272   2355    -18    -21    -40  A    C
ATOM    164  O   ASN A 428       3.384  26.117  31.002  1.00 18.80           A    O
ANISOU  164  O   ASN A 428     2346   2345   2452    -87    -40    -69  A    O
ATOM    165  N   ARG A 429       3.178  24.391  29.582  1.00 18.33           A    N
ANISOU  165  N   ARG A 429     2318   2275   2371    -42    -38    -47  A    N
ATOM    167  CA  ARG A 429       4.441  24.649  28.874  1.00 18.98           A    C
ANISOU  167  CA  ARG A 429     2386   2394   2430    -23     -8    -32  A    C
ATOM    169  CB  ARG A 429       5.653  24.352  29.780  1.00 19.78           A    C
ANISOU  169  CB  ARG A 429     2501   2539   2476     -3    -45    -60  A    C
ATOM    172  CG  ARG A 429       5.760  22.912  30.242  1.00 22.03           A    C
ANISOU  172  CG  ARG A 429     2801   2757   2810    -16      4     26  A    C
ATOM    175  CD  ARG A 429       7.015  22.591  31.061  1.00 25.73           A    C
ANISOU  175  CD  ARG A 429     3174   3365   3234     32   -104     -3  A    C
ATOM    178  NE  ARG A 429       8.241  23.038  30.394  1.00 27.84           A    N
ANISOU  178  NE  ARG A 429     3477   3553   3548    -37     12     77  A    N
ATOM    180  CZ  ARG A 429       9.067  22.276  29.671  1.00 29.91           A    C
ANISOU  180  CZ  ARG A 429     3750   3827   3785     28      2    -36  A    C
ATOM    181  NH1 ARG A 429       8.851  20.976  29.496  1.00 31.32           A    N
ANISOU  181  NH1 ARG A 429     3973   3878   4047     -4     11     -1  A    N
ATOM    184  NH2 ARG A 429      10.143  22.825  29.125  1.00 31.16           A    N
ANISOU  184  NH2 ARG A 429     3955   3964   3918    -21     59     65  A    N
ATOM    187  C   ARG A 429       4.572  23.855  27.578  1.00 18.59           A    C
ANISOU  187  C   ARG A 429     2338   2319   2403    -35    -13    -39  A    C
ATOM    188  O   ARG A 429       3.769  22.957  27.324  1.00 17.92           A    O
ANISOU  188  O   ARG A 429     2141   2343   2323   -126    -43   -100  A    O
ATOM    189  N   ILE A 430       5.576  24.176  26.762  1.00 18.50           A    N
ANISOU  189  N   ILE A 430     2310   2296   2421    -75    -32    -40  A    N
ATOM    191  CA  ILE A 430       5.883  23.381  25.572  1.00 19.36           A    C
ANISOU  191  CA  ILE A 430     2429   2451   2475    -26      8     -3  A    C
ATOM    193  CB  ILE A 430       6.305  24.277  24.350  1.00 19.16           A    C
ANISOU  193  CB  ILE A 430     2389   2413   2478    -29      2      2  A    C
ATOM    195  CG1 ILE A 430       5.082  24.971  23.769  1.00 18.82           A    C
ANISOU  195  CG1 ILE A 430     2379   2336   2433    -52     39     34  A    C
ATOM    198  CD1 ILE A 430       5.354  26.108  22.766  1.00 17.44           A    C
ANISOU  198  CD1 ILE A 430     2197   2173   2255    -15      2    -12  A    C
ATOM    202  CG2 ILE A 430       6.954  23.428  23.250  1.00 20.27           A    C
ANISOU  202  CG2 ILE A 430     2545   2602   2553    -30     52    -11  A    C
ATOM    206  C   ILE A 430       6.958  22.359  25.913  1.00 20.29           A    C
ANISOU  206  C   ILE A 430     2520   2613   2574     -3    -29      9  A    C
ATOM    207  O   ILE A 430       8.054  22.722  26.357  1.00 20.11           A    O
ANISOU  207  O   ILE A 430     2489   2615   2536    -28    -52    -14  A    O
ATOM    208  N   LEU A 431       6.624  21.084  25.721  1.00 21.10           A    N
ANISOU  208  N   LEU A 431     2647   2706   2664    -14    -24    -36  A    N
ATOM    210  CA  LEU A 431       7.550  19.968  25.917  1.00 22.54           A    C
ANISOU  210  CA  LEU A 431     2810   2899   2856     18    -27      8  A    C
ATOM    212  CB  LEU A 431       6.799  18.635  25.897  1.00 22.99           A    C
ANISOU  212  CB  LEU A 431     2892   2919   2922     13    -16    -11  A    C
ATOM    215  CG  LEU A 431       5.887  18.344  27.086  1.00 23.65           A    C
ANISOU  215  CG  LEU A 431     2963   3032   2990      7     -2     16  A    C
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ATOM    217  CD1 LEU A 431       5.020  17.147  26.774  1.00 24.23           A    C
ANISOU  217  CD1 LEU A 431    3139   2966   3100     34      1     19  A    C
ATOM    221  CD2 LEU A 431       6.687  18.129  28.377  1.00 25.23           A    C
ANISOU  221  CD2 LEU A 431    3176   3233   3175      7    -73     17  A    C
ATOM    225  C   LEU A 431       8.604  19.930  24.829  1.00 23.65           A    C
ANISOU  225  C   LEU A 431    2949   3070   2967     30     -5      5  A    C
ATOM    226  O   LEU A 431       9.779  19.671  25.090  1.00 24.47           A    O
ANISOU  226  O   LEU A 431    2919   3312   3064     91     15     44  A    O
ATOM    227  N   GLY A 432       8.181  20.182  23.601  1.00 24.46           A    N
ANISOU  227  N   GLY A 432    3052   3167   3073     23    -23      9  A    N
ATOM    229  CA  GLY A 432       9.096  20.197  22.483  1.00 24.89           A    C
ANISOU  229  CA  GLY A 432    3127   3179   3149     33     14      9  A    C
ATOM    232  C   GLY A 432       8.370  20.267  21.164  1.00 25.37           A    C
ANISOU  232  C   GLY A 432    3191   3230   3215      1     -9     -6  A    C
ATOM    233  O   GLY A 432       7.138  20.300  21.119  1.00 25.05           A    O
ANISOU  233  O   GLY A 432    3135   3225   3156      0      0     -2  A    O
ATOM    234  N   GLU A 433       9.147  20.306  20.092  1.00 26.02           A    N
ANISOU  234  N   GLU A 433    3270   3304   3310     14     34     -7  A    N
ATOM    236  CA  GLU A 433       8.614  20.321  18.743  1.00 26.75           A    C
ANISOU  236  CA  GLU A 433    3355   3403   3403     14      7    -12  A    C
ATOM    238  CB  GLU A 433       9.483  21.193  17.829  1.00 26.94           A    C
ANISOU  238  CB  GLU A 433    3392   3422   3420      2     19     18  A    C
ATOM    241  CG  GLU A 433       9.341  22.703  18.053  1.00 27.97           A    C
ANISOU  241  CG  GLU A 433    3539   3515   3571     14     29    -17  A    C
ATOM    244  CD  GLU A 433      10.146  23.249  19.235  1.00 29.18           A    C
ANISOU  244  CD  GLU A 433    3665   3749   3670     -3    -18    -15  A    C
ATOM    245  OE1 GLU A 433      11.395  23.216  19.160  1.00 30.69           A    O
ANISOU  245  OE1 GLU A 433    3750   4008   3900      2    -10    -14  A    O
ATOM    246  OE2 GLU A 433       9.541  23.737  20.234  1.00 28.38           A    O
ANISOU  246  OE2 GLU A 433    3532   3554   3696     25    -23     16  A    O
ATOM    247  C   GLU A 433       8.571  18.881  18.235  1.00 27.15           A    C
ANISOU  247  C   GLU A 433    3398   3442   3475     10     27    -21  A    C
ATOM    248  O   GLU A 433       9.585  18.323  17.795  1.00 28:41           A    O
ANISOU  248  O   GLU A 433    3499   3633   3663     90     49    -61  A    O
ATOM    249  N   GLY A 434       7.405  18.262  18.331  1.00 26.92           A    N
ANISOU  249  N   GLY A 434    3365   3436   3426     13     11    -13  A    N
ATOM    251  CA  GLY A 434       7.194  16.951  17.757  1.00 26.85           A    C
ANISOU  251  CA  GLY A 434    3389   3412   3398      9      6     -6  A    C
ATOM    254  C   GLY A 434       7.116  16.989  16.237  1.00 26.79           A    C
ANISOU  254  C   GLY A 434    3399   3396   3383      0      8    -15  A    C
ATOM    255  O   GLY A 434       7.243  18.048  15.600  1.00 26.22           A    O
ANISOU  255  O   GLY A 434    3310   3352   3297    -17     52    -68  A    O
ATOM    256  N   PHE A 435       6.896  15.813  15.658  1.00 27.04           A    N
ANISOU  256  N   PHE A 435    3441   3400   3431      8      1    -23  A    N
ATOM    258  CA  PHE A 435       6.782  15.647  14.207  1.00 27.52           A    C
ANISOU  258  CA  PHE A 435    3512   3474   3469     23      7     -7  A    C
ATOM    260  CB  PHE A 435       6.369  14.201  13.893  1.00 28.44           A    C
ANISOU  260  CB  PHE A 435    3608   3563   3632     18      0    -16  A    C
ATOM    263  CG  PHE A 435       6.300  13.899  12.426  1.00 31.95           A    C
ANISOU  263  CG  PHE A 435    4122   4087   3929     16    -14    -47  A    C
ATOM    264  CD1 PHE A 435       7.460  13.682  11.697  1.00 34.08           A    C
ANISOU  264  CD1 PHE A 435    4267   4393   4289     29     77      0  A    C
ATOM    266  CE1 PHE A 435       7.402  13.403  10.343  1.00 35.40           A    C
ANISOU  266  CE1 PHE A 435    4500   4563   4384      4    -24    -22  A    C
ATOM    268  CZ  PHE A 435       6.182  13.346   9.707  1.00 35.84           A    C
ANISOU  268  CZ  PHE A 435    4486   4620   4512     12      3    -13  A    C
ATOM    270  CE2 PHE A 435       5.017  13.571  10.423  1.00 35.45           A    C
ANISOU  270  CE2 PHE A 435    4516   4558   4392      2     -1    -25  A    C
ATOM    272  CD2 PHE A 435       5.081  13.845  11.773  1.00 34.18           A    C
ANISOU  272  CD2 PHE A 435    4255   4412   4317     14    -54    -23  A    C
ATOM    274  C   PHE A 435       5.759  16.589  13.575  1.00 26.36           A    C
ANISOU  274  C   PHE A 435    3364   3309   3342     -1     26    -19  A    C
ATOM    275  O   PHE A 435       6.031  17.213  12.544  1.00 26.24           A    O
ANISOU  275  O   PHE A 435    3407   3284   3278     25     77    -80  A    O
ATOM    276  N   PHE A 436       4.587  16.674  14.208  1.00 25.12           A    N
ANISOU  276  N   PHE A 436    3244   3148   3152     36     13    -19  A    N
ATOM    278  CA  PHE A 436       3.429  17.402  13.675  1.00 24.06           A    C
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ANISOU  278  CA  PHE A 436     3094   3015   3031      8     17    -49  A    C
ATOM    280  CB  PHE A 436       2.124  16.826  14.254  1.00 24.95       A    C
ANISOU  280  CB  PHE A 436     3157   3180   3142     19     12     -9  A    C
ATOM    283  CG  PHE A 436       1.940  15.351  14.009  1.00 28.95       A    C
ANISOU  283  CG  PHE A 436     3718   3538   3741    -72     13    -29  A    C
ATOM    284  CD1 PHE A 436       1.704  14.872  12.729  1.00 31.70       A    C
ANISOU  284  CD1 PHE A 436     4101   4031   3910    -16    -55    -61  A    C
ATOM    286  CE1 PHE A 436       1.541  13.498  12.497  1.00 33.36       A    C
ANISOU  286  CE1 PHE A 436     4325   4099   4251    -26     -5      5  A    C
ATOM    288  CZ  PHE A 436       1.612  12.604  13.552  1.00 33.62       A    C
ANISOU  288  CZ  PHE A 436     4343   4232   4199     14    -31     -2  A    C
ATOM    290  CE2 PHE A 436       1.841  13.069  14.839  1.00 33.02       A    C
ANISOU  290  CE2 PHE A 436     4264   4081   4198    -24    -20    -42  A    C
ATOM    292  CD2 PHE A 436       2.014  14.436  15.062  1.00 31.64       A    C
ANISOU  292  CD2 PHE A 436     4094   3946   3979      3    -42     86  A    C
ATOM    294  C   PHE A 436       3.464  18.893  14.013  1.00 21.43       A    C
ANISOU  294  C   PHE A 436     2729   2772   2639    -19     23    -10  A    C
ATOM    295  O   PHE A 436       2.847  19.695  13.329  1.00 19.47       A    O
ANISOU  295  O   PHE A 436     2560   2502   2335    -26    134    -54  A    O
ATOM    296  N   GLY A 437       4.152  19.237  15.099  1.00 18.75       A    N
ANISOU  296  N   GLY A 437     2360   2386   2379      8     78    -34  A    N
ATOM    298  CA  GLY A 437       4.094  20.576  15.662  1.00 17.07       A    C
ANISOU  298  CA  GLY A 437     2190   2193   2101    -57     32    -19  A    C
ATOM    301  C   GLY A 437       4.424  20.600  17.144  1.00 15.71       A    C
ANISOU  301  C   GLY A 437     2041   1958   1969     -1     43    -18  A    C
ATOM    302  O   GLY A 437       4.907  19.609  17.708  1.00 14.91       A    O
ANISOU  302  O   GLY A 437     1941   1977   1747    -16     42   -135  A    O
ATOM    303  N   GLU A 438       4.123  21.731  17.791  1.00 14.54       A    N
ANISOU  303  N   GLU A 438     1846   1917   1760    -54     62    -10  A    N
ATOM    305  CA  GLU A 438       4.468  21.899  19.191  1.00 14.13       A    C
ANISOU  305  CA  GLU A 438     1791   1840   1738     -6     38     -4  A    C
ATOM    307  CB  GLU A 438       4.184  23.318  19.661  1.00 14.11       A    C
ANISOU  307  CB  GLU A 438     1813   1794   1754    -23     47      6  A    C
ATOM    310  CG  GLU A 438       4.960  24.388  18.916  1.00 16.03       A    C
ANISOU  310  CG  GLU A 438     2081   2028   1979    -54    110     73  A    C
ATOM    313  CD  GLU A 438       6.368  24.563  19.416  1.00 18.92       A    C
ANISOU  313  CD  GLU A 438     2336   2458   2391    -20    -14     61  A    C
ATOM    314  OE1 GLU A 438       6.963  23.598  19.938  1.00 18.75       A    O
ANISOU  314  OE1 GLU A 438     2304   2342   2479      5    183     65  A    O
ATOM    315  OE2 GLU A 438       6.884  25.699  19.299  1.00 22.36       A    O
ANISOU  315  OE2 GLU A 438     2910   2643   2941   -115     55     23  A    O
ATOM    316  C   GLU A 438       3.635  20.925  20.012  1.00 13.22       A    C
ANISOU  316  C   GLU A 438     1653   1763   1605     20     46     -9  A    C
ATOM    317  O   GLU A 438       2.459  20.714  19.735  1.00 13.07       A    O
ANISOU  317  O   GLU A 438     1730   1939   1297    -74     72    -60  A    O
ATOM    318  N   VAL A 439       4.264  20.330  21.014  1.00 12.73       A    N
ANISOU  318  N   VAL A 439     1567   1724   1544    -23     67     16  A    N
ATOM    320  CA  VAL A 439       3.598  19.457  21.963  1.00 11.95       A    C
ANISOU  320  CA  VAL A 439     1504   1539   1497    -17     45      2  A    C
ATOM    322  CB  VAL A 439       4.260  18.070  22.058  1.00 12.24       A    C
ANISOU  322  CB  VAL A 439     1482   1624   1542    -19     10    -21  A    C
ATOM    324  CG1 VAL A 439       3.502  17.197  23.059  1.00 12.64       A    C
ANISOU  324  CG1 VAL A 439     1592   1602   1608     62    -44     85  A    C
ATOM    328  CG2 VAL A 439       4.322  17.420  20.693  1.00 12.04       A    C
ANISOU  328  CG2 VAL A 439     1607   1347   1619    -24    106    -32  A    C
ATOM    332  C   VAL A 439       3.684  20.154  23.315  1.00 11.31       A    C
ANISOU  332  C   VAL A 439     1386   1473   1435    -72    -15     -9  A    C
ATOM    333  O   VAL A 439       4.759  20.594  23.714  1.00 11.12       A    O
ANISOU  333  O   VAL A 439     1313   1556   1355   -141      6    -48  A    O
ATOM    334  N   TYR A 440       2.549  20.243  24.010  1.00 10.48       A    N
ANISOU  334  N   TYR A 440     1319   1294   1369    -93      7    -21  A    N
ATOM    336  CA  TYR A 440       2.442  20.922  25.290  1.00 10.54       A    C
ANISOU  336  CA  TYR A 440     1302   1358   1344    -83    -23     11  A    C
ATOM    338  CB  TYR A 440       1.274  21.906  25.265  1.00 10.13       A    C
ANISOU  338  CB  TYR A 440     1292   1296   1258    -67    -30     -4  A    C
ATOM    341  CG  TYR A 440       1.357  22.990  24.208  1.00  9.13       A    C
ANISOU  341  CG  TYR A 440     1147   1189   1134    -97     51    -19  A    C
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ATOM    342  CD1 TYR A 440      1.833  24.248  24.511  1.00 10.81           A    C
ANISOU  342  CD1 TYR A 440     1463   1310   1334   -114    -80      2  A    C
ATOM    344  CE1 TYR A 440      1.897  25.241  23.543  1.00 12.32           A    C
ANISOU  344  CE1 TYR A 440     1734   1562   1382   -166    -18     76  A    C
ATOM    346  CZ  TYR A 440      1.515  24.972  22.249  1.00 11.63           A    C
ANISOU  346  CZ  TYR A 440     1604   1416   1396    -86      0     91  A    C
ATOM    347  OH  TYR A 440      1.618  25.996  21.316  1.00 13.82           A    O
ANISOU  347  OH  TYR A 440     1852   1892   1504   -314     45    253  A    O
ATOM    349  CE2 TYR A 440      1.065  23.727  21.917  1.00 10.58           A    C
ANISOU  349  CE2 TYR A 440     1356   1517   1147    -56     79    -18  A    C
ATOM    351  CD2 TYR A 440      0.996  22.737  22.891  1.00  9.78           A    C
ANISOU  351  CD2 TYR A 440     1196   1328   1190    -90    -59     -9  A    C
ATOM    353  C   TYR A 440      2.196  19.940  26.414  1.00 11.30           A    C
ANISOU  353  C   TYR A 440     1409   1422   1462   -125    -34      5  A    C
ATOM    354  O   TYR A 440      1.523  18.932  26.226  1.00 11.93           A    O
ANISOU  354  O   TYR A 440     1520   1449   1560   -275   -170    -31  A    O
ATOM    355  N   GLU A 441      2.724  20.239  27.593  1.00 11.57           A    N
ANISOU  355  N   GLU A 441     1424   1507   1464    -80    -52    -40  A    N
ATOM    357  CA  GLU A 441      2.312  19.572  28.810  1.00 12.96           A    C
ANISOU  357  CA  GLU A 441     1633   1646   1645    -13     -4    -27  A    C
ATOM    359  CB  GLU A 441      3.418  19.564  29.862  1.00 14.31           A    C
ANISOU  359  CB  GLU A 441     1748   1885   1804     24    -44    -27  A    C
ATOM    362  CG  GLU A 441      3.021  18.766  31.094  1.00 18.27           A    C
ANISOU  362  CG  GLU A 441     2323   2331   2285    -75     92     40  A    C
ATOM    365  CD  GLU A 441      4.123  18.618  32.115  1.00 23.03           A    C
ANISOU  365  CD  GLU A 441     2875   3010   2863     41   -140     55  A    C
ATOM    366  OE1 GLU A 441      5.321  18.774  31.760  1.00 27.63           A    O
ANISOU  366  OE1 GLU A 441     3187   3829   3479     15     35    124  A    O
ATOM    367  OE2 GLU A 441      3.786  18.342  33.285  1.00 26.26           A    O
ANISOU  367  OE2 GLU A 441     3301   3543   3134     26     99     36  A    O
ATOM    368  C   GLU A 441      1.140  20.351  29.342  1.00 12.30           A    C
ANISOU  368  C   GLU A 441     1566   1580   1527      5    -14    -32  A    C
ATOM    369  O   GLU A 441      1.151  21.596  29.341  1.00 12.57           A    O
ANISOU  369  O   GLU A 441     1640   1579   1554    -29     34    -28  A    O
ATOM    370  N   GLY A 442      0.118  19.634  29.769  1.00 12.18           A    N
ANISOU  370  N   GLY A 442     1611   1531   1486     14     21    -26  A    N
ATOM    372  CA  GLY A 442     -1.001  20.257  30.452  1.00 12.50           A    C
ANISOU  372  CA  GLY A 442     1603   1609   1534     15     12    -27  A    C
ATOM    375  C   GLY A 442     -1.686  19.352  31.454  1.00 12.64           A    C
ANISOU  375  C   GLY A 442     1609   1602   1592      0    -13      2  A    C
ATOM    376  O   GLY A 442     -1.237  18.246  31.752  1.00 12.27           A    O
ANISOU  376  O   GLY A 442     1662   1541   1457    -49    -21   -114  A    O
ATOM    377  N   VAL A 443     -2.807  19.848  31.963  1.00 13.10           A    N
ANISOU  377  N   VAL A 443     1693   1666   1616     27     35      7  A    N
ATOM    379  CA  VAL A 443     -3.639  19.103  32.889  1.00 13.71           A    C
ANISOU  379  CA  VAL A 443     1738   1730   1741     13     14     18  A    C
ATOM    381  CB  VAL A 443     -3.578  19.703  34.298  1.00 14.27           A    C
ANISOU  381  CB  VAL A 443     1788   1845   1786    -11      3     -5  A    C
ATOM    383  CG1 VAL A 443     -4.581  19.007  35.233  1.00 14.54           A    C
ANISOU  383  CG1 VAL A 443     1859   1914   1752     22     34     38  A    C
ATOM    387  CG2 VAL A 443     -2.181  19.561  34.859  1.00 14.32           A    C
ANISOU  387  CG2 VAL A 443     1795   1872   1773      5    -10    -59  A    C
ATOM    391  C   VAL A 443     -5.074  19.067  32.403  1.00 13.17           A    C
ANISOU  391  C   VAL A 443     1686   1660   1657     20     35     41  A    C
ATOM    392  O   VAL A 443     -5.677  20.094  32.118  1.00 13.26           A    O
ANISOU  392  O   VAL A 443     1742   1581   1716     67     43     55  A    O
ATOM    393  N   TYR A 444     -5.619  17.864  32.342  1.00 12.72           A    N
ANISOU  393  N   TYR A 444     1678   1575   1578     54     22     66  A    N
ATOM    395  CA  TYR A 444     -6.976  17.622  31.944  1.00 12.83           A    C
ANISOU  395  CA  TYR A 444     1637   1633   1604     43     50     91  A    C
ATOM    397  CB  TYR A 444     -7.041  16.415  31.015  1.00 13.36           A    C
ANISOU  397  CB  TYR A 444     1722   1673   1680     21     40    108  A    C
ATOM    400  CG  TYR A 444     -8.425  15.829  30.850  1.00 14.22           A    C
ANISOU  400  CG  TYR A 444     1777   1870   1756     -4     32     88  A    C
ATOM    401  CD1 TYR A 444     -9.527  16.644  30.596  1.00 15.71           A    C
ANISOU  401  CD1 TYR A 444     1985   2023   1959     40     13     81  A    C
ATOM    403  CE1 TYR A 444    -10.793  16.095  30.460  1.00 16.75           A    C
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ANISOU  403  CE1 TYR A 444     2039   2253   2071      7    -72     99  A    C
ATOM    405  CZ  TYR A 444     -10.954  14.728  30.556  1.00 17.08      A    C
ANISOU  405  CZ  TYR A 444     2181   2265   2042     -6      6     32  A    C
ATOM    406  OH  TYR A 444     -12.193  14.156  30.422  1.00 20.54      A    O
ANISOU  406  OH  TYR A 444     2562   2665   2575   -236    -38     65  A    O
ATOM    408  CE2 TYR A 444      -9.890  13.917  30.810  1.00 16.31      A    C
ANISOU  408  CE2 TYR A 444     2117   2000   2077    -72      6     64  A    C
ATOM    410  CD2 TYR A 444      -8.631  14.462  30.943  1.00 16.63      A    C
ANISOU  410  CD2 TYR A 444     2057   2040   2221    -12     36     28  A    C
ATOM    412  C   TYR A 444      -7.735  17.350  33.218  1.00 13.67      A    C
ANISOU  412  C   TYR A 444     1762   1727   1703     52     59     79  A    C
ATOM    413  O   TYR A 444      -7.379  16.436  33.953  1.00 13.60      A    O
ANISOU  413  O   TYR A 444     1743   1767   1656     42     51    153  A    O
ATOM    414  N   THR A 445      -8.749  18.172  33.485  1.00 13.86      A    N
ANISOU  414  N   THR A 445     1723   1781   1762     60     72     36  A    N
ATOM    416  CA  THR A 445      -9.588  18.011  34.665  1.00 14.76      A    C
ANISOU  416  CA  THR A 445     1875   1910   1821      0     43     60  A    C
ATOM    418  CB  THR A 445      -9.814  19.361  35.380  1.00 14.26      A    C
ANISOU  418  CB  THR A 445     1780   1837   1800     41     58     72  A    C
ATOM    420  OG1 THR A 445      -8.561  19.916  35.777  1.00 15.78      A    O
ANISOU  420  OG1 THR A 445     2033   1974   1989    -69    -16     55  A    O
ATOM    422  CG2 THR A 445     -10.566  19.197  36.721  1.00 14.65      A    C
ANISOU  422  CG2 THR A 445     1946   1852   1768     10     14     41  A    C
ATOM    426  C   THR A 445     -10.892  17.475  34.117  1.00 15.56      A    C
ANISOU  426  C   THR A 445     1926   2046   1936      0     23     72  A    C
ATOM    427  O   THR A 445     -11.581  18.169  33.379  1.00 15.80      A    O
ANISOU  427  O   THR A 445     1908   2128   1966     30     45    188  A    O
ATOM    428  N   ASN A 446     -11.225  16.237  34.441  1.00 16.06      A    N
ANISOU  428  N   ASN A 446     2074   2069   1957    -13     24     44  A    N
ATOM    430  CA  ASN A 446     -12.499  15.684  34.022  1.00 16.90      A    C
ANISOU  430  CA  ASN A 446     2187   2180   2054    -42     -2     24  A    C
ATOM    432  CB  ASN A 446     -12.425  14.151  33.997  1.00 16.14      A    C
ANISOU  432  CB  ASN A 446     2134   2071   1925    -31     23     36  A    C
ATOM    435  CG  ASN A 446     -12.366  13.525  35.395  1.00 15.76      A    C
ANISOU  435  CG  ASN A 446     2058   2019   1908    -28     12     -3  A    C
ATOM    436  OD1 ASN A 446     -12.610  14.174  36.394  1.00 13.92      A    O
ANISOU  436  OD1 ASN A 446     1872   1816   1598    -97    -66    137  A    O
ATOM    437  ND2 ASN A 446     -12.059  12.255  35.442  1.00 16.63      A    N
ANISOU  437  ND2 ASN A 446     2320   2031   1967    -36    -35    113  A    N
ATOM    440  C   ASN A 446     -13.662  16.235  34.871  1.00 18.01      A    C
ANISOU  440  C   ASN A 446     2317   2317   2205    -35     36      5  A    C
ATOM    441  O   ASN A 446     -13.461  17.105  35.722  1.00 17.82      A    O
ANISOU  441  O   ASN A 446     2312   2331   2128   -126     64     22  A    O
ATOM    442  N   HIS A 447     -14.882  15.778  34.606  1.00 19.72      A    N
ANISOU  442  N   HIS A 447     2522   2530   2441    -64    -23     -8  A    N
ATOM    444  CA  HIS A 447     -16.070  16.349  35.251  1.00 21.09      A    C
ANISOU  444  CA  HIS A 447     2665   2717   2628    -16     -5     20  A    C
ATOM    446  CB  HIS A 447     -17.347  15.890  34.530  1.00 22.10      A    C
ANISOU  446  CB  HIS A 447     2780   2841   2775    -49    -29    -18  A    C
ATOM    449  CG  HIS A 447     -17.554  16.527  33.187  1.00 25.24      A    C
ANISOU  449  CG  HIS A 447     3287   3216   3084     19    -31     71  A    C
ATOM    450  ND1 HIS A 447     -18.753  16.448  32.507  1.00 28.07      A    N
ANISOU  450  ND1 HIS A 447     3513   3631   3517    -67   -110     37  A    N
ATOM    452  CE1 HIS A 447     -18.647  17.092  31.357  1.00 29.07      A    C
ANISOU  452  CE1 HIS A 447     3675   3756   3613    -61    -32     65  A    C
ATOM    454  NE2 HIS A 447     -17.425  17.586  31.267  1.00 28.72      A    N
ANISOU  454  NE2 HIS A 447     3615   3729   3566    -38    -30     64  A    N
ATOM    456  CD2 HIS A 447     -16.720  17.244  32.397  1.00 27.27      A    C
ANISOU  456  CD2 HIS A 447     3427   3467   3464    -61     10     69  A    C
ATOM    458  C   HIS A 447     -16.170  16.022  36.758  1.00 20.82      A    C
ANISOU  458  C   HIS A 447     2634   2677   2598    -14    -13     -1  A    C
ATOM    459  O   HIS A 447     -16.936  16.668  37.496  1.00 21.25      A    O
ANISOU  459  O   HIS A 447     2642   2781   2649    -12    -47     19  A    O
ATOM    460  N   LYS A 448     -15.400  15.022  37.192  1.00 20.49      A    N
ANISOU  460  N   LYS A 448     2626   2626   2530    -48    -32     41  A    N
ATOM    462  CA  LYS A 448     -15.304  14.653  38.608  1.00 20.17      A    C
ANISOU  462  CA  LYS A 448     2586   2580   2496    -44    -26      4  A    C
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ATOM    464  CB  LYS A 448     -15.058  13.150  38.734  1.00 20.12           A    C
ANISOU  464  CB  LYS A 448     2596   2562   2485    -16    -16     21  A    C
ATOM    467  CG  LYS A 448     -16.243  12.328  38.264  1.00 20.68           A    C
ANISOU  467  CG  LYS A 448     2613   2656   2586    -31    -30      0  A    C
ATOM    470  CD  LYS A 448     -15.881  10.871  38.151  1.00 21.62           A    C
ANISOU  470  CD  LYS A 448     2803   2688   2721    -50    -67     63  A    C
ATOM    473  CE  LYS A 448     -16.979  10.064  37.483  1.00 21.84           A    C
ANISOU  473  CE  LYS A 448     2806   2767   2725    -25    -36      5  A    C
ATOM    476  NZ  LYS A 448     -16.595   8.631  37.433  1.00 21.44           A    N
ANISOU  476  NZ  LYS A 448     2818   2691   2636    -26    -64     64  A    N
ATOM    480  C   LYS A 448     -14.212  15.416  39.367  1.00 19.90           A    C
ANISOU  480  C   LYS A 448     2560   2556   2443    -71    -18     29  A    C
ATOM    481  O   LYS A 448     -14.055  15.234  40.581  1.00 20.18           A    O
ANISOU  481  O   LYS A 448     2647   2614   2407   -120    -37     45  A    O
ATOM    482  N   GLY A 449     -13.466  16.261  38.660  1.00 18.93           A    N
ANISOU  482  N   GLY A 449     2429   2436   2325    -48    -23     16  A    N
ATOM    484  CA  GLY A 449     -12.438  17.082  39.268  1.00 18.33           A    C
ANISOU  484  CA  GLY A 449     2333   2359   2270     -3     22     17  A    C
ATOM    487  C   GLY A 449     -11.099  16.384  39.325  1.00 18.11           A    C
ANISOU  487  C   GLY A 449     2304   2334   2243    -10     11     25  A    C
ATOM    488  O   GLY A 449     -10.153  16.929  39.872  1.00 18.44           A    O
ANISOU  488  O   GLY A 449     2343   2383   2280    -17    -13     19  A    O
ATOM    489  N   GLU A 450     -11.015  15.186  38.758  1.00 17.86           A    N
ANISOU  489  N   GLU A 450     2254   2294   2235    -21     -6     48  A    N
ATOM    491  CA  GLU A 450      -9.760  14.439  38.722  1.00 18.01           A    C
ANISOU  491  CA  GLU A 450     2280   2315   2249    -18     22     15  A    C
ATOM    493  CB  GLU A 450     -10.031  12.991  38.356  1.00 18.11           A    C
ANISOU  493  CB  GLU A 450     2303   2300   2276     -2     -3      4  A    C
ATOM    496  CG  GLU A 450     -10.952  12.287  39.340  1.00 19.27           A    C
ANISOU  496  CG  GLU A 450     2475   2472   2374    -45     -5     60  A    C
ATOM    499  CD  GLU A 450     -11.219  10.857  38.943  1.00 21.94           A    C
ANISOU  499  CD  GLU A 450     2934   2634   2768    -79    -38     20  A    C
ATOM    500  OE1 GLU A 450     -11.672  10.634  37.795  1.00 23.68           A    O
ANISOU  500  OE1 GLU A 450     3178   2995   2822   -111    -66     77  A    O
ATOM    501  OE2 GLU A 450     -10.962   9.957  39.774  1.00 22.58           A    O
ANISOU  501  OE2 GLU A 450     3007   2808   2765   -104   -108    137  A    O
ATOM    502  C   GLU A 450      -8.799  15.046  37.713  1.00 18.31           A    C
ANISOU  502  C   GLU A 450     2319   2346   2292    -46     -2     50  A    C
ATOM    503  O   GLU A 450      -9.191  15.323  36.588  1.00 17.45           A    O
ANISOU  503  O   GLU A 450     2142   2295   2192    -73      9     49  A    O
ATOM    504  N   LYS A 451      -7.542  15.226  38.122  1.00 18.88           A    N
ANISOU  504  N   LYS A 451     2349   2450   2374    -27      3     49  A    N
ATOM    506  CA  LYS A 451      -6.537  15.886  37.292  1.00 19.30           A    C
ANISOU  506  CA  LYS A 451     2420   2474   2436    -11      8     41  A    C
ATOM    508  CB  LYS A 451      -5.773  16.933  38.101  1.00 19.90           A    C
ANISOU  508  CB  LYS A 451     2504   2553   2503    -25      0     25  A    C
ATOM    511  CG  LYS A 451      -6.656  18.007  38.734  1.00 21.63           A    C
ANISOU  511  CG  LYS A 451     2709   2729   2779      2     48    -12  A    C
ATOM    514  CD  LYS A 451      -6.191  19.431  38.405  1.00 23.25           A    C
ANISOU  514  CD  LYS A 451     2959   2905   2968    -52      0     53  A    C
ATOM    517  CE  LYS A 451      -7.065  20.474  39.069  1.00 23.83           A    C
ANISOU  517  CE  LYS A 451     2991   3052   3009    -15     -6      5  A    C
ATOM    520  NZ  LYS A 451      -7.846  21.294  38.116  1.00 24.29           A    N
ANISOU  520  NZ  LYS A 451     3103   3063   3062    -44      7     63  A    N
ATOM    524  C   LYS A 451      -5.576  14.860  36.707  1.00 19.37           A    C
ANISOU  524  C   LYS A 451     2436   2512   2411     -9      1     43  A    C
ATOM    525  O   LYS A 451      -4.954  14.066  37.431  1.00 19.54           A    O
ANISOU  525  O   LYS A 451     2436   2534   2454     17    -16     87  A    O
ATOM    526  N   ILE A 452      -5.470  14.881  35.383  1.00 19.06           A    N
ANISOU  526  N   ILE A 452     2411   2463   2365    -24     21     50  A    N
ATOM    528  CA  ILE A 452      -4.694  13.928  34.622  1.00 19.44           A    C
ANISOU  528  CA  ILE A 452     2448   2471   2464    -14      8     59  A    C
ATOM    530  CB  ILE A 452      -5.684  13.140  33.686  1.00 20.36           A    C
ANISOU  530  CB  ILE A 452     2588   2603   2544    -48    -29     27  A    C
ATOM    532  CG1 ILE A 452      -6.674  12.316  34.541  1.00 22.71           A    C
ANISOU  532  CG1 ILE A 452     2879   2905   2845    -80     23     68  A    C
ATOM    535  CD1 ILE A 452      -7.858  11.768  33.782  1.00 24.16           A    C
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ANISOU  535  CD1 ILE A 452     3037   3086   3054    -90    -39     50  A    C
ATOM    539  CG2 ILE A 452      -4.975  12.233  32.713  1.00 20.63      A    C
ANISOU  539  CG2 ILE A 452     2573   2651   2614    -15    -20     36  A    C
ATOM    543  C   ILE A 452      -3.654  14.733  33.834  1.00 17.96      A    C
ANISOU  543  C   ILE A 452     2251   2313   2261     47      8     55  A    C
ATOM    544  O   ILE A 452      -4.010  15.652  33.113  1.00 17.20      A    O
ANISOU  544  O   ILE A 452     2194   2146   2193    131     84     90  A    O
ATOM    545  N   ASN A 453      -2.371  14.422  33.996  1.00 16.81      A    N
ANISOU  545  N   ASN A 453     2139   2108   2137     76     -9     45  A    N
ATOM    547  CA  ASN A 453      -1.331  15.050  33.194  1.00 16.18      A    C
ANISOU  547  CA  ASN A 453     2022   2087   2036     66    -52     18  A    C
ATOM    549  CB  ASN A 453       0.070  14.751  33.747  1.00 17.02      A    C
ANISOU  549  CB  ASN A 453     2092   2199   2173     85    -58     36  A    C
ATOM    552  CG  ASN A 453       0.234  15.222  35.166  1.00 19.63      A    C
ANISOU  552  CG  ASN A 453     2501   2585   2370      9    -62    -41  A    C
ATOM    553  OD1 ASN A 453       0.683  14.462  36.040  1.00 24.36      A    O
ANISOU  553  OD1 ASN A 453     3128   3251   2877     94   -220    164  A    O
ATOM    554  ND2 ASN A 453      -0.154  16.457  35.421  1.00 18.71      A    N
ANISOU  554  ND2 ASN A 453     2282   2542   2281     10   -178     18  A    N
ATOM    557  C   ASN A 453      -1.415  14.572  31.758  1.00 14.71      A    C
ANISOU  557  C   ASN A 453     1820   1874   1895     74    -27     46  A    C
ATOM    558  O   ASN A 453      -1.539  13.379  31.497  1.00 15.20      A    O
ANISOU  558  O   ASN A 453     1937   1971   1865     86   -101     37  A    O
ATOM    559  N   VAL A 454      -1.367  15.525  30.836  1.00 12.89      A    N
ANISOU  559  N   VAL A 454     1613   1593   1688     50    -48      0  A    N
ATOM    561  CA  VAL A 454      -1.511  15.246  29.418  1.00 11.46      A    C
ANISOU  561  CA  VAL A 454     1412   1412   1528     60    -41     23  A    C
ATOM    563  CB  VAL A 454      -2.910  15.649  28.880  1.00 10.74      A    C
ANISOU  563  CB  VAL A 454     1336   1273   1468     40    -43     14  A    C
ATOM    565  CG1 VAL A 454      -3.991  14.806  29.534  1.00 11.37      A    C
ANISOU  565  CG1 VAL A 454     1323   1411   1587     82     -8     21  A    C
ATOM    569  CG2 VAL A 454      -3.191  17.144  29.047  1.00 10.27      A    C
ANISOU  569  CG2 VAL A 454     1352   1251   1296     24    -24     -6  A    C
ATOM    573  C   VAL A 454      -0.432  15.913  28.586  1.00 11.10      A    C
ANISOU  573  C   VAL A 454     1375   1356   1487     28    -75      9  A    C
ATOM    574  O   VAL A 454       0.158  16.934  28.982  1.00 11.62      A    O
ANISOU  574  O   VAL A 454     1341   1411   1664     32   -123   -108  A    O
ATOM    575  N   ALA A 455      -0.164  15.290  27.444  1.00 10.28      A    N
ANISOU  575  N   ALA A 455     1293   1177   1436     48    -86    -43  A    N
ATOM    577  CA  ALA A 455       0.601  15.841  26.361  1.00 10.79      A    C
ANISOU  577  CA  ALA A 455     1369   1251   1478    -37    -90      8  A    C
ATOM    579  CB  ALA A 455       1.607  14.858  25.836  1.00 10.88      A    C
ANISOU  579  CB  ALA A 455     1292   1424   1418    -44     25     27  A    C
ATOM    583  C   ALA A 455      -0.407  16.225  25.275  1.00 11.22      A    C
ANISOU  583  C   ALA A 455     1454   1377   1432   -102   -122     32  A    C
ATOM    584  O   ALA A 455      -1.261  15.418  24.872  1.00 13.07      A    O
ANISOU  584  O   ALA A 455     1746   1421   1799   -243   -207    112  A    O
ATOM    585  N   VAL A 456      -0.345  17.468  24.840  1.00 10.13      A    N
ANISOU  585  N   VAL A 456     1323   1231   1293    -95    -15      0  A    N
ATOM    587  CA  VAL A 456      -1.261  17.960  23.835  1.00 10.58      A    C
ANISOU  587  CA  VAL A 456     1347   1340   1331    -21     -8    -11  A    C
ATOM    589  CB  VAL A 456      -2.037  19.199  24.300  1.00  9.96      A    C
ANISOU  589  CB  VAL A 456     1317   1285   1181    -26     -1    -13  A    C
ATOM    591  CG1 VAL A 456      -3.004  19.641  23.192  1.00 11.36      A    C
ANISOU  591  CG1 VAL A 456     1448   1516   1350     42    -66     -1  A    C
ATOM    595  CG2 VAL A 456      -2.804  18.879  25.581  1.00 11.32      A    C
ANISOU  595  CG2 VAL A 456     1438   1590   1271    -62     18      3  A    C
ATOM    599  C   VAL A 456      -0.521  18.262  22.553  1.00 11.04      A    C
ANISOU  599  C   VAL A 456     1483   1337   1373    -99      4     20  A    C
ATOM    600  O   VAL A 456       0.326  19.144  22.517  1.00 11.55      A    O
ANISOU  600  O   VAL A 456     1503   1375   1511   -173     61    -40  A    O
ATOM    601  N   LYS A 457      -0.828  17.505  21.501  1.00 10.92      A    N
ANISOU  601  N   LYS A 457     1460   1352   1337   -155    -12    -36  A    N
ATOM    603  CA  LYS A 457      -0.189  17.668  20.205  1.00 12.29      A    C
ANISOU  603  CA  LYS A 457     1578   1564   1526    -86     13    -46  A    C
ATOM    605  CB  LYS A 457      -0.165  16.343  19.447  1.00 12.94      A    C
ANISOU  605  CB  LYS A 457     1646   1617   1650    -78     16   -121  A    C
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ATOM    608  CG  LYS A 457       0.446  15.205  20.233  1.00 17.77           A    C
ANISOU  608  CG  LYS A 457    2283   2217   2251     51    -21     73  A    C
ATOM    611  CD  LYS A 457       0.979  14.101  19.312  1.00 22.35           A    C
ANISOU  611  CD  LYS A 457    2962   2729   2800    108     29   -131  A    C
ATOM    614  CE  LYS A 457      -0.007  12.979  19.123  1.00 25.98           A    C
ANISOU  614  CE  LYS A 457    3284   3293   3291    -78      1      2  A    C
ATOM    617  NZ  LYS A 457       0.634  11.893  18.327  1.00 28.65           A    N
ANISOU  617  NZ  LYS A 457    3675   3488   3720    123     12    -70  A    N
ATOM    621  C   LYS A 457      -0.959  18.664  19.387  1.00 11.53           A    C
ANISOU  621  C   LYS A 457    1538   1480   1363   -102     17    -71  A    C
ATOM    622  O   LYS A 457      -2.186  18.621  19.333  1.00 11.18           A    O
ANISOU  622  O   LYS A 457    1602   1472   1174   -173    -41    -49  A    O
ATOM    623  N   THR A 458      -0.228  19.579  18.763  1.00 11.68           A    N
ANISOU  623  N   THR A 458    1544   1514   1379   -112     59    -67  A    N
ATOM    625  CA  THR A 458      -0.809  20.529  17.844  1.00 11.93           A    C
ANISOU  625  CA  THR A 458    1562   1549   1422    -55     13    -86  A    C
ATOM    627  CB  THR A 458      -0.725  21.966  18.383  1.00 12.32           A    C
ANISOU  627  CB  THR A 458    1602   1575   1502    -45     27    -84  A    C
ATOM    629  OG1 THR A 458       0.647  22.381  18.478  1.00 11.89           A    O
ANISOU  629  OG1 THR A 458    1577   1768   1173   -132    119   -164  A    O
ATOM    631  CG2 THR A 458      -1.281  22.017  19.799  1.00 10.96           A    C
ANISOU  631  CG2 THR A 458    1506   1256   1402    -84    -12    -48  A    C
ATOM    635  C   THR A 458      -0.114  20.446  16.505  1.00 13.06           A    C
ANISOU  635  C   THR A 458    1684   1720   1558    -50     23    -88  A    C
ATOM    636  O   THR A 458       0.942  19.832  16.386  1.00 12.37           A    O
ANISOU  636  O   THR A 458    1679   1806   1213    -53    111   -209  A    O
ATOM    637  N   CYS A 459      -0.721  21.088  15.521  1.00 14.61           A    N
ANISOU  637  N   CYS A 459    1964   1845   1742    -44      0    -64  A    N
ATOM    639  CA  CYS A 459      -0.188  21.077  14.165  1.00 15.99           A    C
ANISOU  639  CA  CYS A 459    2103   2069   1903   -100     10    -46  A    C
ATOM    641  CB  CYS A 459      -1.264  20.724  13.138  1.00 17.53           A    C
ANISOU  641  CB  CYS A 459    2227   2423   2008    -37    -47    -39  A    C
ATOM    644  SG  CYS A 459      -1.594  18.929  13.033  1.00 22.86           A    S
ANISOU  644  SG  CYS A 459    2952   3255   2478   -791   -155   -532  A    S
ATOM    645  C   CYS A 459       0.429  22.421  13.871  1.00 15.76           A    C
ANISOU  645  C   CYS A 459    2067   2029   1890    -33    -49    -29  A    C
ATOM    646  O   CYS A 459      -0.171  23.463  14.136  1.00 14.36           A    O
ANISOU  646  O   CYS A 459    1973   1890   1590    -69   -114    -87  A    O
ATOM    647  N   LYS A 460       1.645  22.365  13.349  1.00 15.95           A    N
ANISOU  647  N   LYS A 460    2113   2056   1890     -9    -41    -59  A    N
ATOM    649  CA  LYS A 460       2.361  23.536  12.911  1.00 17.02           A    C
ANISOU  649  CA  LYS A 460    2198   2157   2112    -48    -11    -38  A    C
ATOM    651  CB  LYS A 460       3.765  23.181  12.424  1.00 17.45           A    C
ANISOU  651  CB  LYS A 460    2237   2213   2179    -27      7      7  A    C
ATOM    654  CG  LYS A 460       3.838  22.242  11.232  1.00 20.13           A    C
ANISOU  654  CG  LYS A 460    2645   2538   2462    -36     -7    -72  A    C
ATOM    657  CD  LYS A 460       5.301  21.915  10.910  1.00 23.80           A    C
ANISOU  657  CD  LYS A 460    2908   3102   3031     26     48    -61  A    C
ATOM    660  CE  LYS A 460       5.857  20.843  11.829  1.00 25.78           A    C
ANISOU  660  CE  LYS A 460    3269   3291   3234      4    -31      8  A    C
ATOM    663  NZ  LYS A 460       7.303  20.538  11.561  1.00 27.95           A    N
ANISOU  663  NZ  LYS A 460    3409   3621   3590     52      3     -7  A    N
ATOM    667  C   LYS A 460       1.574  24.265  11.847  1.00 16.99           A    C
ANISOU  667  C   LYS A 460    2162   2160   2132    -34    -19    -27  A    C
ATOM    668  O   LYS A 460       0.721  23.670  11.157  1.00 17.16           A    O
ANISOU  668  O   LYS A 460    2149   2281   2089    -98    -50    -66  A    O
ATOM    669  N   LYS A 461       1.837  25.561  11.719  1.00 17.39           A    N
ANISOU  669  N   LYS A 461    2225   2204   2175    -47    -19    -52  A    N
ATOM    671  CA  LYS A 461       1.047  26.390  10.833  1.00 17.93           A    C
ANISOU  671  CA  LYS A 461    2281   2258   2273    -28    -23     -8  A    C
ATOM    673  CB  LYS A 461       1.414  27.867  10.985  1.00 18.42           A    C
ANISOU  673  CB  LYS A 461    2355   2350   2292      0     -8    -15  A    C
ATOM    676  CG  LYS A 461       2.717  28.200  10.442  1.00 18.49           A    C
ANISOU  676  CG  LYS A 461    2340   2328   2358    -46    -45      7  A    C
ATOM    679  CD  LYS A 461       3.000  29.687  10.608  1.00 17.75           A    C
ANISOU  679  CD  LYS A 461    2247   2259   2239    -72     -2      8  A    C
ATOM    682  CE  LYS A 461       4.327  29.964  10.021  1.00 17.68           A    C
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ANISOU  682  CE  LYS A 461     2220   2316   2182     34     12     -2  A    C
ATOM    685  NZ  LYS A 461       4.595  31.378   9.966  1.00 15.93        A    N
ANISOU  685  NZ  LYS A 461     1954   2170   1928   -119     95   -100  A    N
ATOM    689  C   LYS A 461       1.175  25.903   9.392  1.00 18.50        A    C
ANISOU  689  C   LYS A 461     2362   2352   2315    -26     11     16  A    C
ATOM    690  O   LYS A 461       0.235  26.036   8.618  1.00 18.56        A    O
ANISOU  690  O   LYS A 461     2350   2395   2305    -37    -11      8  A    O
ATOM    691  N   ASP A 462       2.309  25.285   9.060  1.00 19.44        A    N
ANISOU  691  N   ASP A 462     2459   2469   2457    -34      0      5  A    N
ATOM    693  CA  ASP A 462       2.521  24.705   7.737  1.00 20.50        A    C
ANISOU  693  CA  ASP A 462     2615   2583   2591    -22     -2    -34  A    C
ATOM    695  CB  ASP A 462       4.011  24.747   7.340  1.00 21.57        A    C
ANISOU  695  CB  ASP A 462     2697   2744   2751     -6      2    -44  A    C
ATOM    698  CG  ASP A 462       4.234  24.606   5.838  1.00 24.85        A    C
ANISOU  698  CG  ASP A 462     3199   3201   3038    -17     17    -52  A    C
ATOM    699  OD1 ASP A 462       3.548  25.288   5.060  1.00 28.28        A    O
ANISOU  699  OD1 ASP A 462     3690   3668   3386     85    -51     39  A    O
ATOM    700  OD2 ASP A 462       5.087  23.840   5.340  1.00 28.72        A    O
ANISOU  700  OD2 ASP A 462     3522   3761   3627    106     77   -169  A    O
ATOM    701  C   ASP A 462       1.984  23.267   7.746  1.00 20.27        A    C
ANISOU  701  C   ASP A 462     2566   2573   2561      0    -42    -48  A    C
ATOM    702  O   ASP A 462       2.745  22.306   7.894  1.00 22.31        A    O
ANISOU  702  O   ASP A 462     2814   2842   2819     33    -30   -149  A    O
ATOM    703  N   CME A 463       0.709  23.148   7.402  1.00 19.42        A    N
ANISOU  703  N   CME A 463     2456   2468   2452    -17    -24    -70  A    N
ATOM    706  CA  CME A 463       0.071  21.860   7.475  1.00 18.40        A    C
ANISOU  706  CA  CME A 463     2334   2392   2264    -16    -29    -36  A    C
ATOM    708  CB  CME A 463      -0.254  21.485   8.939  1.00 19.10        A    C
ANISOU  708  CB  CME A 463     2395   2503   2359     -7    -38    -59  A    C
ATOM    711  SG  CME A 463      -0.977  19.896   9.168  1.00 23.43        A    S
ANISOU  711  SG  CME A 463     3199   3069   2632   -199   -114   -144  A    S
ATOM    712  S2  CME A 463       0.497  18.544   9.074  1.00 28.04        A    S
ANISOU  712  S2  CME A 463     3750   3133   3767    -94   -119   -278  A    S
ATOM    713  C2  CME A 463       2.017  19.054   8.364  1.00 30.33        A    C
ANISOU  713  C2  CME A 463     3927   3790   3807    -48     62    -51  A    C
ATOM    716  C1  CME A 463       3.166  18.838   9.310  1.00 33.78        A    C
ANISOU  716  C1  CME A 463     4277   4290   4268     22    -49    -13  A    C
ATOM    718  O1  CME A 463       4.145  19.578   9.206  1.00 36.82        A    O
ANISOU  718  O1  CME A 463     4541   4709   4738    -68     14     -4  A    O
ATOM    719  C   CME A 463      -1.280  21.972   6.924  1.00 16.38        A    C
ANISOU  719  C   CME A 463     2122   2097   2002    -23      0    -43  A    C
ATOM    720  O   CME A 463      -2.086  22.802   7.149  1.00 14.95        A    O
ANISOU  720  O   CME A 463     2000   1969   1709   -105    -36   -112  A    O
ATOM    722  N   THR A 464      -1.287  21.329   5.764  1.00 14.94        A    N
ANISOU  722  N   THR A 464     1857   1986   1830     -7    -27    -64  A    N
ATOM    724  CA  THR A 464      -2.339  21.522   4.798  1.00 14.07        A    C
ANISOU  724  CA  THR A 464     1784   1892   1669    -25     -5    -99  A    C
ATOM    726  CB  THR A 464      -1.907  21.016   3.430  1.00 14.07        A    C
ANISOU  726  CB  THR A 464     1763   1982   1601    -92    -27    -89  A    C
ATOM    728  OG1 THR A 464      -1.504  19.649   3.548  1.00 13.52        A    O
ANISOU  728  OG1 THR A 464     1653   2136   1348   -200    -63   -217  A    O
ATOM    730  CG2 THR A 464      -0.682  21.763   2.914  1.00 15.07        A    C
ANISOU  730  CG2 THR A 464     1880   2134   1712    -83     40   -130  A    C
ATOM    734  C   THR A 464      -3.501  20.713   5.263  1.00 13.24        A    C
ANISOU  734  C   THR A 464     1697   1807   1525     13      1   -117  A    C
ATOM    735  O   THR A 464      -3.355  19.782   6.037  1.00 12.68        A    O
ANISOU  735  O   THR A 464     1617   1760   1440    -16    -50   -274  A    O
ATOM    736  N   LEU A 465      -4.673  21.066   4.767  1.00 12.73        A    N
ANISOU  736  N   LEU A 465     1606   1808   1421     15    -33   -154  A    N
ATOM    738  CA  LEU A 465      -5.853  20.278   5.063  1.00 12.88        A    C
ANISOU  738  CA  LEU A 465     1663   1728   1500    -32     -6    -57  A    C
ATOM    740  CB  LEU A 465      -7.067  20.931   4.430  1.00 12.55        A    C
ANISOU  740  CB  LEU A 465     1625   1683   1458     -2      5    -12  A    C
ATOM    743  CG  LEU A 465      -7.490  22.259   5.046  1.00 12.91        A    C
ANISOU  743  CG  LEU A 465     1669   1664   1571    -86     56    -30  A    C
ATOM    745  CD1 LEU A 465      -8.576  22.885   4.210  1.00 15.25        A    C
ANISOU  745  CD1 LEU A 465     1932   2033   1828     72     18    -84  A    C
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ATOM    749  CD2 LEU A 465      -7.940  22.071   6.486  1.00 14.13           A    C
ANISOU  749  CD2 LEU A 465     1832   1916   1621     -7     84    -88  A    C
ATOM    753  C   LEU A 465      -5.713  18.851   4.555  1.00 13.30           A    C
ANISOU  753  C   LEU A 465     1696   1784   1572    -58    -52    -54  A    C
ATOM    754  O   LEU A 465      -6.233  17.919   5.137  1.00 13.10           A    O
ANISOU  754  O   LEU A 465     1757   1772   1448   -150   -106   -125  A    O
ATOM    755  N   ASP A 466      -5.001  18.688   3.447  1.00 14.29           A    N
ANISOU  755  N   ASP A 466     1732   1956   1740    -59    -15   -103  A    N
ATOM    757  CA  ASP A 466      -4.649  17.365   2.933  1.00 15.75           A    C
ANISOU  757  CA  ASP A 466     1964   2021   1998    -31    -13    -52  A    C
ATOM    759  CB  ASP A 466      -3.768  17.595   1.694  1.00 16.19           A    C
ANISOU  759  CB  ASP A 466     2013   2092   2046      1      7    -64  A    C
ATOM    762  CG  ASP A 466      -3.400  16.334   0.957  1.00 18.38           A    C
ANISOU  762  CG  ASP A 466     2366   2283   2335     45     38    -63  A    C
ATOM    763  OD1 ASP A 466      -3.566  15.220   1.482  1.00 18.27           A    O
ANISOU  763  OD1 ASP A 466     2282   2225   2432    137     40    -28  A    O
ATOM    764  OD2 ASP A 466      -2.891  16.411  -0.190  1.00 21.14           A    O
ANISOU  764  OD2 ASP A 466     2704   2875   2450    178     57     -3  A    O
ATOM    765  C   ASP A 466      -3.957  16.536   4.027  1.00 16.82           A    C
ANISOU  765  C   ASP A 466     2101   2140   2146     15      6    -71  A    C
ATOM    766  O   ASP A 466      -4.444  15.491   4.438  1.00 16.81           A    O
ANISOU  766  O   ASP A 466     1934   2293   2159      0     21    -96  A    O
ATOM    767  N   ASN A 467      -2.832  17.026   4.534  1.00 18.07           A    N
ANISOU  767  N   ASN A 467     2214   2341   2311    -35    -11    -57  A    N
ATOM    769  CA  ASN A 467      -2.121  16.313   5.582  1.00 19.78           A    C
ANISOU  769  CA  ASN A 467     2477   2498   2538      5    -28    -32  A    C
ATOM    771  CB  ASN A 467      -0.737  16.928   5.794  1.00 20.56           A    C
ANISOU  771  CB  ASN A 467     2537   2625   2648    -32    -31    -20  A    C
ATOM    774  CG  ASN A 467       0.229  16.574   4.672  1.00 22.62           A    C
ANISOU  774  CG  ASN A 467     2775   2889   2929     37     68    -61  A    C
ATOM    775  OD1 ASN A 467       0.859  17.452   4.057  1.00 23.81           A    O
ANISOU  775  OD1 ASN A 467     2798   2995   3252     76    149    -58  A    O
ATOM    776  ND2 ASN A 467       0.331  15.278   4.381  1.00 24.98           A    N
ANISOU  776  ND2 ASN A 467     3031   3041   3416     68     39    -58  A    N
ATOM    779  C   ASN A 467      -2.899  16.237   6.892  1.00 20.16           A    C
ANISOU  779  C   ASN A 467     2520   2560   2578    -21    -41    -14  A    C
ATOM    780  O   ASN A 467      -2.808  15.241   7.614  1.00 20.23           A    O
ANISOU  780  O   ASN A 467     2562   2539   2583    -41    -18    -24  A    O
ATOM    781  N   LYS A 468      -3.681  17.266   7.201  1.00 20.54           A    N
ANISOU  781  N   LYS A 468     2605   2564   2635    -26    -40    -31  A    N
ATOM    783  CA  LYS A 468      -4.477  17.259   8.422  1.00 21.30           A    C
ANISOU  783  CA  LYS A 468     2715   2684   2695    -42     -4     -4  A    C
ATOM    785  CB  LYS A 468      -5.207  18.591   8.633  1.00 21.59           A    C
ANISOU  785  CB  LYS A 468     2728   2722   2752      6      5     32  A    C
ATOM    788  CG  LYS A 468      -4.377  19.632   9.351  1.00 24.20           A    C
ANISOU  788  CG  LYS A 468     3026   3103   3062    -27    -13    -39  A    C
ATOM    791  CD  LYS A 468      -5.128  20.926   9.566  1.00 25.91           A    C
ANISOU  791  CD  LYS A 468     3276   3253   3313     48     20    -28  A    C
ATOM    794  CE  LYS A 468      -4.182  22.044   9.994  1.00 27.19           A    C
ANISOU  794  CE  LYS A 468     3404   3437   3490    -51      3    -23  A    C
ATOM    797  NZ  LYS A 468      -4.900  23.299  10.354  1.00 28.40           A    N
ANISOU  797  NZ  LYS A 468     3622   3639   3529     41     41     -9  A    N
ATOM    801  C   LYS A 468      -5.495  16.116   8.427  1.00 21.72           A    C
ANISOU  801  C   LYS A 468     2785   2719   2748    -68      7     22  A    C
ATOM    802  O   LYS A 468      -5.729  15.526   9.476  1.00 22.45           A    O
ANISOU  802  O   LYS A 468     2914   2767   2846    -79     -3     80  A    O
ATOM    803  N   GLU A 469      -6.078  15.798   7.269  1.00 21.72           A    N
ANISOU  803  N   GLU A 469     2775   2723   2754    -37    -26     54  A    N
ATOM    805  CA  GLU A 469      -7.038  14.687   7.163  1.00 22.61           A    C
ANISOU  805  CA  GLU A 469     2875   2844   2869    -47     -9     16  A    C
ATOM    807  CB  GLU A 469      -7.649  14.613   5.759  1.00 23.02           A    C
ANISOU  807  CB  GLU A 469     2889   2932   2924    -20    -16     -5  A    C
ATOM    810  CG  GLU A 469      -8.749  13.562   5.624  1.00 24.14           A    C
ANISOU  810  CG  GLU A 469     3042   3075   3054    -76    -36     51  A    C
ATOM    813  CD  GLU A 469      -8.315  12.246   4.988  1.00 27.42           A    C
ANISOU  813  CD  GLU A 469     3495   3409   3512     42      0    -28  A    C
ATOM    814  OE1 GLU A 469      -7.176  12.125   4.492  1.00 29.73           A    O
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ANISOU  814  OE1 GLU A 469     3673   3893   3729    -41     77     19  A    O
ATOM    815  OE2 GLU A 469      -9.131  11.292   4.989  1.00 29.95      A    O
ANISOU  815  OE2 GLU A 469     3640   3810   3927   -122     -5    -21  A    O
ATOM    816  C   GLU A 469      -6.367  13.346   7.498  1.00 23.42      A    C
ANISOU  816  C   GLU A 469     2990   2925   2984    -23    -15      5  A    C
ATOM    817  O   GLU A 469      -6.947  12.495   8.184  1.00 23.03      A    O
ANISOU  817  O   GLU A 469     2973   2852   2922    -19    -17      4  A    O
ATOM    818  N   LYS A 470      -5.152  13.163   7.002  1.00 24.57      A    N
ANISOU  818  N   LYS A 470     3089   3097   3150    -20     -4    -14  A    N
ATOM    820  CA  LYS A 470      -4.380  11.953   7.273  1.00 25.96      A    C
ANISOU  820  CA  LYS A 470     3290   3239   3333     -4    -10      2  A    C
ATOM    822  CB  LYS A 470      -3.026  12.008   6.559  1.00 26.85      A    C
ANISOU  822  CB  LYS A 470     3374   3364   3463     -2     21      0  A    C
ATOM    825  CG  LYS A 470      -3.074  12.031   5.046  1.00 28.91      A    C
ANISOU  825  CG  LYS A 470     3680   3666   3637    -10     -9    -25  A    C
ATOM    828  CD  LYS A 470      -1.669  12.255   4.471  1.00 30.89      A    C
ANISOU  828  CD  LYS A 470     3826   3954   3958     -5     35     17  A    C
ATOM    831  CE  LYS A 470      -1.675  12.400   2.954  1.00 32.45      A    C
ANISOU  831  CE  LYS A 470     4115   4158   4055    -20     17      3  A    C
ATOM    834  NZ  LYS A 470      -1.310  13.782   2.473  1.00 33.67      A    N
ANISOU  834  NZ  LYS A 470     4283   4241   4268    -30    -19     17  A    N
ATOM    838  C   LYS A 470      -4.152  11.789   8.774  1.00 26.18      A    C
ANISOU  838  C   LYS A 470     3302   3289   3355     -7      7     -5  A    C
ATOM    839  O   LYS A 470      -4.404  10.731   9.339  1.00 27.01      A    O
ANISOU  839  O   LYS A 470     3425   3344   3493     32      7     35  A    O
ATOM    840  N   PHE A 471      -3.695  12.853   9.421  1.00 25.95      A    N
ANISOU  840  N   PHE A 471     3261   3255   3343    -10      2     -8  A    N
ATOM    842  CA  PHE A 471      -3.362  12.817  10.845  1.00 25.82      A    C
ANISOU  842  CA  PHE A 471     3257   3251   3302    -17     -1     22  A    C
ATOM    844  CB  PHE A 471      -2.694  14.122  11.277  1.00 26.48      A    C
ANISOU  844  CB  PHE A 471     3375   3316   3369    -26    -17      1  A    C
ATOM    847  CG  PHE A 471      -1.430  14.433  10.539  1.00 29.15      A    C
ANISOU  847  CG  PHE A 471     3612   3787   3677     -3     37     21  A    C
ATOM    848  CD1 PHE A 471      -0.745  13.453   9.816  1.00 31.05      A    C
ANISOU  848  CD1 PHE A 471     3928   3921   3945     45     32    -44  A    C
ATOM    850  CE1 PHE A 471       0.418  13.767   9.134  1.00 32.18      A    C
ANISOU  850  CE1 PHE A 471     4022   4066   4138    -23     51    -12  A    C
ATOM    852  CZ  PHE A 471       0.913  15.059   9.174  1.00 32.01      A    C
ANISOU  852  CZ  PHE A 471     4055   4034   4073      6     22     24  A    C
ATOM    854  CE2 PHE A 471       0.234  16.031   9.882  1.00 31.70      A    C
ANISOU  854  CE2 PHE A 471     4012   4053   3979    -58     29     14  A    C
ATOM    856  CD2 PHE A 471      -0.930  15.722  10.554  1.00 30.89      A    C
ANISOU  856  CD2 PHE A 471     3892   3928   3915    -27      6    -36  A    C
ATOM    858  C   PHE A 471      -4.561  12.604  11.736  1.00 25.07      A    C
ANISOU  858  C   PHE A 471     3156   3158   3210     -6    -21      6  A    C
ATOM    859  O   PHE A 471      -4.459  11.957  12.773  1.00 24.28      A    O
ANISOU  859  O   PHE A 471     3004   3006   3214   -103    -44     40  A    O
ATOM    860  N   MET A 472      -5.689  13.182  11.351  1.00 24.49      A    N
ANISOU  860  N   MET A 472     3096   3084   3123    -25    -17     23  A    N
ATOM    862  CA  MET A 472      -6.891  13.091  12.155  1.00 24.34      A    C
ANISOU  862  CA  MET A 472     3089   3066   3094    -10      3     16  A    C
ATOM    864  CB  MET A 472      -7.927  14.118  11.710  1.00 24.75      A    C
ANISOU  864  CB  MET A 472     3163   3134   3106     15     -8     24  A    C
ATOM    867  CG  MET A 472      -7.468  15.528  11.941  1.00 27.04      A    C
ANISOU  867  CG  MET A 472     3505   3408   3362    -20    -50    -18  A    C
ATOM    870  SD  MET A 472      -7.230  15.809  13.673  1.00 30.11      A    S
ANISOU  870  SD  MET A 472     4137   3871   3430    -73    -82     28  A    S
ATOM    871  CE  MET A 472      -8.902  16.260  14.143  1.00 30.30      A    C
ANISOU  871  CE  MET A 472     3964   3785   3761    -30    -40    -16  A    C
ATOM    875  C   MET A 472      -7.434  11.683  12.043  1.00 23.47      A    C
ANISOU  875  C   MET A 472     2948   2948   3018     -5     -2    -10  A    C
ATOM    876  O   MET A 472      -7.835  11.105  13.046  1.00 22.54      A    O
ANISOU  876  O   MET A 472     2782   2692   3087    -28     21    -16  A    O
ATOM    877  N   SER A 473      -7.397  11.134  10.835  1.00 23.29      A    N
ANISOU  877  N   SER A 473     2910   2915   3022     10      5     10  A    N
ATOM    879  CA  SER A 473      -7.778   9.741  10.595  1.00 23.99      A    C
ANISOU  879  CA  SER A 473     3050   2995   3069    -34     15    -23  A    C
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ATOM    881  CB  SER A 473      -7.530   9.365   9.131  1.00 24.56           A    C
ANISOU  881  CB  SER A 473    3154   3079   3098    -30      4    -34  A    C
ATOM    884  OG  SER A 473      -8.335  10.139   8.276  1.00 27.20           A    O
ANISOU  884  OG  SER A 473    3512   3346   3477     37      1    -39  A    O
ATOM    886  C   SER A 473      -7.010   8.788  11.488  1.00 23.83           A    C
ANISOU  886  C   SER A 473    3037   2969   3047    -42     38    -29  A    C
ATOM    887  O   SER A 473      -7.588   7.883  12.086  1.00 23.99           A    O
ANISOU  887  O   SER A 473    3186   2840   3086   -112    117    -86  A    O
ATOM    888  N   GLU A 474      -5.702   8.990  11.573  1.00 23.71           A    N
ANISOU  888  N   GLU A 474    3023   2935   3047    -33     -2     -6  A    N
ATOM    890  CA  GLU A 474      -4.829   8.150  12.382  1.00 23.37           A    C
ANISOU  890  CA  GLU A 474    2931   2935   3012    -36     15      7  A    C
ATOM    892  CB  GLU A 474      -3.360   8.466  12.059  1.00 24.34           A    C
ANISOU  892  CB  GLU A 474    2989   3061   3198    -30     -1      4  A    C
ATOM    895  CG  GLU A 474      -2.941   8.037  10.651  1.00 27.51           A    C
ANISOU  895  CG  GLU A 474    3550   3482   3420     12     -3    -55  A    C
ATOM    898  CD  GLU A 474      -1.783   8.853  10.090  1.00 32.17           A    C
ANISOU  898  CD  GLU A 474    3968   4118   4136    -73     80     27  A    C
ATOM    899  OE1 GLU A 474      -1.100   9.553  10.871  1.00 34.14           A    O
ANISOU  899  OE1 GLU A 474    4302   4334   4336    -34    -37    -99  A    O
ATOM    900  OE2 GLU A 474      -1.547   8.794   8.859  1.00 35.20           A    O
ANISOU  900  OE2 GLU A 474    4516   4598   4258      0     27    -19  A    O
ATOM    901  C   GLU A 474      -5.108   8.341  13.861  1.00 21.79           A    C
ANISOU  901  C   GLU A 474    2710   2682   2887    -22      3     -5  A    C
ATOM    902  O   GLU A 474      -5.080   7.382  14.633  1.00 20.36           A    O
ANISOU  902  O   GLU A 474    2363   2556   2814   -137     72     75  A    O
ATOM    903  N   ALA A 475      -5.394   9.568  14.267  1.00 20.31           A    N
ANISOU  903  N   ALA A 475    2491   2500   2723    -73     41     22  A    N
ATOM    905  CA  ALA A 475      -5.705   9.834  15.661  1.00 19.50           A    C
ANISOU  905  CA  ALA A 475    2479   2348   2581    -50    -14    -20  A    C
ATOM    907  CB  ALA A 475      -5.826  11.348  15.893  1.00 19.18           A    C
ANISOU  907  CB  ALA A 475    2454   2292   2539    -14    -30     -4  A    C
ATOM    911  C   ALA A 475      -6.986   9.113  16.131  1.00 19.35           A    C
ANISOU  911  C   ALA A 475    2492   2328   2531    -47     -3    -25  A    C
ATOM    912  O   ALA A 475      -7.046   8.634  17.256  1.00 18.32           A    O
ANISOU  912  O   ALA A 475    2470   1974   2514   -193    -54    -98  A    O
ATOM    913  N   VAL A 476      -7.999   9.054  15.271  1.00 19.06           A    N
ANISOU  913  N   VAL A 476    2442   2313   2486    -61     49    -62  A    N
ATOM    915  CA  VAL A 476      -9.257   8.358  15.587  1.00 19.09           A    C
ANISOU  915  CA  VAL A 476    2437   2331   2484    -36     28    -40  A    C
ATOM    917  CB  VAL A 476     -10.349   8.645  14.514  1.00 19.07           A    C
ANISOU  917  CB  VAL A 476    2419   2337   2487    -16     25    -39  A    C
ATOM    919  CG1 VAL A 476     -11.592   7.797  14.731  1.00 20.08           A    C
ANISOU  919  CG1 VAL A 476    2462   2561   2607     -3     26    -64  A    C
ATOM    923  CG2 VAL A 476     -10.720  10.137  14.528  1.00 19.60           A    C
ANISOU  923  CG2 VAL A 476    2453   2432   2561    -14      2    -40  A    C
ATOM    927  C   VAL A 476      -8.985   6.865  15.752  1.00 18.83           A    C
ANISOU  927  C   VAL A 476    2407   2308   2439    -46     54    -57  A    C
ATOM    928  O   VAL A 476      -9.568   6.231  16.613  1.00 18.22           A    O
ANISOU  928  O   VAL A 476    2315   2188   2420   -172    161   -183  A    O
ATOM    929  N   ILE A 477      -8.057   6.311  14.975  1.00 18.97           A    N
ANISOU  929  N   ILE A 477    2394   2359   2454    -51     89    -45  A    N
ATOM    931  CA  ILE A 477      -7.686   4.906  15.167  1.00 18.91           A    C
ANISOU  931  CA  ILE A 477    2373   2323   2488    -46     76    -38  A    C
ATOM    933  CB  ILE A 477      -6.741   4.397  14.062  1.00 19.56           A    C
ANISOU  933  CB  ILE A 477    2480   2428   2522    -32     85    -17  A    C
ATOM    935  CG1 ILE A 477      -7.467   4.333  12.726  1.00 20.91           A    C
ANISOU  935  CG1 ILE A 477    2585   2631   2728    -18     17    -29  A    C
ATOM    938  CD1 ILE A 477      -6.537   4.159  11.530  1.00 22.97           A    C
ANISOU  938  CD1 ILE A 477    2952   2899   2875    -24     97    -40  A    C
ATOM    942  CG2 ILE A 477      -6.178   3.022  14.439  1.00 20.66           A    C
ANISOU  942  CG2 ILE A 477    2590   2596   2661    -19    102      6  A    C
ATOM    946  C   ILE A 477      -7.042   4.729  16.538  1.00 18.42           A    C
ANISOU  946  C   ILE A 477    2339   2226   2431    -12     63    -80  A    C
ATOM    947  O   ILE A 477      -7.390   3.842  17.310  1.00 17.83           A    O
ANISOU  947  O   ILE A 477    2273   2119   2382   -161    157   -199  A    O
ATOM    948  N   MET A 478      -6.117   5.617  16.866  1.00 18.34           A    N
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ANISOU  948  N   MET A 478     2292   2195   2482    -71     41      2  A    N
ATOM    950  CA  MET A 478      -5.446   5.557  18.143  1.00 19.38      A    C
ANISOU  950  CA  MET A 478     2492   2344   2527    -62     -2    -24  A    C
ATOM    952  CB  MET A 478      -4.323   6.616  18.231  1.00 20.22      A    C
ANISOU  952  CB  MET A 478     2563   2437   2681    -72    -34     -7  A    C
ATOM    955  CG  MET A 478      -3.109   6.353  17.341  1.00 22.57      A    C
ANISOU  955  CG  MET A 478     2917   2795   2863    -86     75    -23  A    C
ATOM    958  SD  MET A 478      -2.232   4.756  17.613  1.00 24.48      A    S
ANISOU  958  SD  MET A 478     3183   2881   3237   -176     60     31  A    S
ATOM    959  CE  MET A 478      -1.864   4.806  19.305  1.00 23.71      A    C
ANISOU  959  CE  MET A 478     3066   2860   3080    -32      0     45  A    C
ATOM    963  C   MET A 478      -6.413   5.699  19.301  1.00 18.90      A    C
ANISOU  963  C   MET A 478     2434   2267   2479   -110    -45    -50  A    C
ATOM    964  O   MET A 478      -6.239   5.043  20.309  1.00 18.91      A    O
ANISOU  964  O   MET A 478     2513   2153   2518   -197   -100    -77  A    O
ATOM    965  N   LYS A 479      -7.421   6.562  19.159  1.00 18.61      A    N
ANISOU  965  N   LYS A 479     2405   2246   2419   -113    -51    -27  A    N
ATOM    967  CA  LYS A 479      -8.463   6.735  20.169  1.00 19.16      A    C
ANISOU  967  CA  LYS A 479     2498   2386   2393    -81     -7    -48  A    C
ATOM    969  CB  LYS A 479      -9.507   7.770  19.717  1.00 20.24      A    C
ANISOU  969  CB  LYS A 479     2670   2500   2517    -54    -20    -21  A    C
ATOM    972  CG  LYS A 479     -10.627   8.023  20.746  1.00 22.66      A    C
ANISOU  972  CG  LYS A 479     2887   2894   2826    -53     68    -67  A    C
ATOM    975  CD  LYS A 479     -11.477   9.232  20.413  1.00 26.49      A    C
ANISOU  975  CD  LYS A 479     3344   3355   3365     83      0      8  A    C
ATOM    978  CE  LYS A 479     -12.825   9.209  21.157  1.00 28.20      A    C
ANISOU  978  CE  LYS A 479     3530   3639   3546    -21     78      2  A    C
ATOM    981  NZ  LYS A 479     -13.953   8.782  20.289  1.00 30.33      A    N
ANISOU  981  NZ  LYS A 479     3791   3947   3784    -59    -22    -26  A    N
ATOM    985  C   LYS A 479      -9.159   5.407  20.529  1.00 18.39      A    C
ANISOU  985  C   LYS A 479     2426   2311   2249    -99      4    -23  A    C
ATOM    986  O   LYS A 479      -9.546   5.172  21.685  1.00 18.52      A    O
ANISOU  986  O   LYS A 479     2491   2351   2192   -180    -49   -146  A    O
ATOM    987  N   ASN A 480      -9.356   4.564  19.523  1.00 16.96      A    N
ANISOU  987  N   ASN A 480     2237   2099   2106    -34     18    -14  A    N
ATOM    989  CA  ASN A 480     -10.026   3.286  19.703  1.00 16.98      A    C
ANISOU  989  CA  ASN A 480     2160   2145   2147    -13     -7    -11  A    C
ATOM    991  CB  ASN A 480     -10.698   2.858  18.401  1.00 16.39      A    C
ANISOU  991  CB  ASN A 480     2076   2060   2090    -37      4    -52  A    C
ATOM    994  CG  ASN A 480     -11.934   3.639  18.112  1.00 15.29      A    C
ANISOU  994  CG  ASN A 480     1897   2026   1885   -129      0    -70  A    C
ATOM    995  OD1 ASN A 480     -11.942   4.557  17.280  1.00 18.43      A    O
ANISOU  995  OD1 ASN A 480     2446   2331   2223   -208    -96     46  A    O
ATOM    996  ND2 ASN A 480     -13.011   3.303  18.816  1.00 13.78      A    N
ANISOU  996  ND2 ASN A 480     1582   1892   1762   -370   -146   -128  A    N
ATOM    999  C   ASN A 480      -9.129   2.159  20.204  1.00 17.53      A    C
ANISOU  999  C   ASN A 480     2223   2210   2226     19    -15      8  A    C
ATOM   1000  O   ASN A 480      -9.622   1.111  20.641  1.00 18.79      A    O
ANISOU 1000  O   ASN A 480     2245   2368   2526    -45      0    -13  A    O
ATOM   1001  N   LEU A 481      -7.820   2.343  20.127  1.00 18.67      A    N
ANISOU 1001  N   LEU A 481     2339   2379   2372    -11    -18     36  A    N
ATOM   1003  CA  LEU A 481      -6.906   1.361  20.703  1.00 19.92      A    C
ANISOU 1003  CA  LEU A 481     2491   2490   2588      9      4     21  A    C
ATOM   1005  CB  LEU A 481      -5.514   1.472  20.095  1.00 19.88      A    C
ANISOU 1005  CB  LEU A 481     2462   2479   2611    -37      7     31  A    C
ATOM   1008  CG  LEU A 481      -5.337   0.959  18.682  1.00 19.33      A    C
ANISOU 1008  CG  LEU A 481     2395   2422   2526    -44      2     21  A    C
ATOM   1010  CD1 LEU A 481      -3.960   1.337  18.187  1.00 19.58      A    C
ANISOU 1010  CD1 LEU A 481     2355   2496   2587    -44     42    -36  A    C
ATOM   1014  CD2 LEU A 481      -5.512  -0.541  18.559  1.00 18.61      A    C
ANISOU 1014  CD2 LEU A 481     2201   2342   2528    -48     -8    -53  A    C
ATOM   1018  C   LEU A 481      -6.826   1.556  22.207  1.00 20.75      A    C
ANISOU 1018  C   LEU A 481     2607   2605   2671     -7    -31     19  A    C
ATOM   1019  O   LEU A 481      -6.351   2.579  22.698  1.00 23.44      A    O
ANISOU 1019  O   LEU A 481     3130   2817   2960    -75    -85     30  A    O
ATOM   1020  N   ASP A 482      -7.252   0.544  22.936  1.00 19.94      A    N
ANISOU 1020  N   ASP A 482     2354   2547   2673    -12      4     43  A    N
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ATOM   1022  CA  ASP A 482      -7.259   0.567  24.385  1.00 20.20           A    C
ANISOU 1022  CA  ASP A 482    2423   2593   2658     -6    -14     -1  A    C
ATOM   1024  CB  ASP A 482      -8.699   0.585  24.928  1.00 21.21           A    C
ANISOU 1024  CB  ASP A 482    2492   2737   2829     -7     28     36  A    C
ATOM   1027  CG  ASP A 482      -8.795   1.086  26.367  1.00 24.55           A    C
ANISOU 1027  CG  ASP A 482    3026   3244   3055     -4     29    -54  A    C
ATOM   1028  OD1 ASP A 482      -7.776   1.153  27.090  1.00 26.94           A    O
ANISOU 1028  OD1 ASP A 482    3169   3589   3477     68     42    -84  A    O
ATOM   1029  OD2 ASP A 482      -9.894   1.432  26.884  1.00 29.24           A    O
ANISOU 1029  OD2 ASP A 482    3376   3929   3802    104    152    -37  A    O
ATOM   1030  C   ASP A 482      -6.532  -0.698  24.788  1.00 19.47           A    C
ANISOU 1030  C   ASP A 482    2366   2458   2573    -81    -51     37  A    C
ATOM   1031  O   ASP A 482      -7.070  -1.795  24.722  1.00 21.32           A    O
ANISOU 1031  O   ASP A 482    2652   2592   2854   -109   -142     65  A    O
ATOM   1032  N   HIS A 483      -5.265  -0.533  25.136  1.00 16.58           A    N
ANISOU 1032  N   HIS A 483    2011   2099   2188    -22    -11    -23  A    N
ATOM   1034  CA  HIS A 483      -4.430  -1.613  25.569  1.00 15.45           A    C
ANISOU 1034  CA  HIS A 483    1977   1944   1946    -48      1      0  A    C
ATOM   1036  CB  HIS A 483      -3.614  -2.176  24.393  1.00 15.27           A    C
ANISOU 1036  CB  HIS A 483    1873   1981   1945    -27      9    -68  A    C
ATOM   1039  CG  HIS A 483      -2.972  -3.478  24.705  1.00 15.11           A    C
ANISOU 1039  CG  HIS A 483    2091   1955   1696    -45     -4     -1  A    C
ATOM   1040  ND1 HIS A 483      -1.888  -3.587  25.541  1.00 14.86           A    N
ANISOU 1040  ND1 HIS A 483    1922   1862   1862    -43     20    -94  A    N
ATOM   1042  CE1 HIS A 483      -1.587  -4.860  25.707  1.00 16.29           A    C
ANISOU 1042  CE1 HIS A 483    2204   1904   2080    116     12   -177  A    C
ATOM   1044  NE2 HIS A 483      -2.413  -5.584  24.975  1.00 16.13           A    N
ANISOU 1044  NE2 HIS A 483    2252   2054   1821    -78    -44     89  A    N
ATOM   1046  CD2 HIS A 483      -3.281  -4.744  24.323  1.00 16.71           A    C
ANISOU 1046  CD2 HIS A 483    2200   1975   2174     40    -78    -81  A    C
ATOM   1048  C   HIS A 483      -3.501  -1.061  26.647  1.00 14.08           A    C
ANISOU 1048  C   HIS A 483    1731   1775   1845      0     23     -4  A    C
ATOM   1049  O   HIS A 483      -3.031   0.075  26.517  1.00 13.86           A    O
ANISOU 1049  O   HIS A 483    1538   1815   1913     -9    136    -45  A    O
ATOM   1050  N   PRO A 484      -3.250  -1.822  27.717  1.00 13.40           A    N
ANISOU 1050  N   PRO A 484    1676   1608   1806     -6     56    -36  A    N
ATOM   1051  CA  PRO A 484      -2.360  -1.331  28.765  1.00 13.42           A    C
ANISOU 1051  CA  PRO A 484    1685   1656   1757     68     41      0  A    C
ATOM   1053  CB  PRO A 484      -2.332  -2.483  29.788  1.00 14.58           A    C
ANISOU 1053  CB  PRO A 484    1899   1792   1849    -11     77     30  A    C
ATOM   1056  CG  PRO A 484      -3.446  -3.345  29.452  1.00 15.97           A    C
ANISOU 1056  CG  PRO A 484    2026   1962   2077    -23    -86      4  A    C
ATOM   1059  CD  PRO A 484      -3.849  -3.127  28.069  1.00 13.57           A    C
ANISOU 1059  CD  PRO A 484    1721   1667   1766    -21     84    -36  A    C
ATOM   1062  C   PRO A 484      -0.961  -0.972  28.281  1.00 12.89           A    C
ANISOU 1062  C   PRO A 484    1678   1551   1668     15     21      1  A    C
ATOM   1063  O   PRO A 484      -0.298  -0.240  28.987  1.00 12.93           A    O
ANISOU 1063  O   PRO A 484    1688   1539   1684     29    -31    -89  A    O
ATOM   1064  N   HIS A 485      -0.504  -1.486  27.135  1.00 12.02           A    N
ANISOU 1064  N   HIS A 485    1536   1444   1587     14     25     16  A    N
ATOM   1066  CA  HIS A 485       0.846  -1.194  26.667  1.00 11.59           A    C
ANISOU 1066  CA  HIS A 485    1455   1436   1513     68     76      6  A    C
ATOM   1068  CB  HIS A 485       1.704  -2.445  26.786  1.00 12.42           A    C
ANISOU 1068  CB  HIS A 485    1506   1595   1618     36     40    -21  A    C
ATOM   1071  CG  HIS A 485       1.737  -2.953  28.196  1.00 16.90           A    C
ANISOU 1071  CG  HIS A 485    2175   2294   1952    290    168    192  A    C
ATOM   1072  ND1 HIS A 485       2.884  -3.185  28.896  1.00 24.89           A    N
ANISOU 1072  ND1 HIS A 485    3030   3698   2726   -296   -189    291  A    N
ATOM   1074  CE1 HIS A 485       2.579  -3.596  30.118  1.00 23.33           A    C
ANISOU 1074  CE1 HIS A 485    3028   3348   2487    -30      7    120  A    C
ATOM   1076  NE2 HIS A 485       1.285  -3.609  30.242  1.00 20.63           A    N
ANISOU 1076  NE2 HIS A 485    2810   2815   2211     35    -75    218  A    N
ATOM   1078  CD2 HIS A 485       0.730  -3.153  29.076  1.00 23.26           A    C
ANISOU 1078  CD2 HIS A 485    2913   3335   2589   -224     19    322  A    C
ATOM   1080  C   HIS A 485       0.856  -0.583  25.281  1.00 10.76           A    C
ANISOU 1080  C   HIS A 485    1357   1307   1423     42    -20    -15  A    C
ATOM   1081  O   HIS A 485       1.791  -0.771  24.511  1.00 10.12           A    O
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ANISOU 1081  O   HIS A 485     1239   1166   1439     70    -24    -33  A    O
ATOM   1082  N   ILE A 486      -0.198   0.176  24.993  1.00  9.75       A    N
ANISOU 1082  N   ILE A 486     1225   1255   1224    101     32    -30  A    N
ATOM   1084  CA  ILE A 486      -0.232   1.097  23.843  1.00 10.19       A    C
ANISOU 1084  CA  ILE A 486     1387   1160   1322     41    -28    -33  A    C
ATOM   1086  CB  ILE A 486      -1.268   0.655  22.782  1.00  9.74       A    C
ANISOU 1086  CB  ILE A 486     1305   1111   1284     74    -35    -40  A    C
ATOM   1088  CG1 ILE A 486      -0.894  -0.735  22.230  1.00 11.70       A    C
ANISOU 1088  CG1 ILE A 486     1556   1206   1680     62    -40      6  A    C
ATOM   1091  CD1 ILE A 486      -1.888  -1.277  21.230  1.00 12.79       A    C
ANISOU 1091  CD1 ILE A 486     1576   1542   1738     -5    -71    -11  A    C
ATOM   1095  CG2 ILE A 486      -1.356   1.695  21.677  1.00 11.01       A    C
ANISOU 1095  CG2 ILE A 486     1373   1557   1253     35     44      0  A    C
ATOM   1099  C   ILE A 486      -0.575   2.503  24.346  1.00  9.96       A    C
ANISOU 1099  C   ILE A 486     1290   1200   1291     72     -2    -51  A    C
ATOM   1100  O   ILE A 486      -1.434   2.673  25.223  1.00 10.61       A    O
ANISOU 1100  O   ILE A 486     1394   1177   1461    137     68   -112  A    O
ATOM   1101  N   VAL A 487       0.123   3.496  23.828  1.00 10.88       A    N
ANISOU 1101  N   VAL A 487     1433   1284   1415     68    -32    -33  A    N
ATOM   1103  CA  VAL A 487      -0.119   4.870  24.267  1.00 11.41       A    C
ANISOU 1103  CA  VAL A 487     1449   1356   1527     39     22    -31  A    C
ATOM   1105  CB  VAL A 487       0.729   5.886  23.464  1.00 11.90       A    C
ANISOU 1105  CB  VAL A 487     1523   1349   1647     40     23    -31  A    C
ATOM   1107  CG1 VAL A 487       2.203   5.669  23.775  1.00 10.94       A    C
ANISOU 1107  CG1 VAL A 487     1527   1338   1290    -75      6    -92  A    C
ATOM   1111  CG2 VAL A 487       0.431   5.805  21.981  1.00 14.05       A    C
ANISOU 1111  CG2 VAL A 487     1875   1617   1845     82     40     35  A    C
ATOM   1115  C   VAL A 487      -1.613   5.215  24.177  1.00 12.14       A    C
ANISOU 1115  C   VAL A 487     1487   1487   1637     25     13    -34  A    C
ATOM   1116  O   VAL A 487      -2.320   4.793  23.253  1.00 12.52       A    O
ANISOU 1116  O   VAL A 487     1452   1584   1720    174    -17    -47  A    O
ATOM   1117  N   LYS A 488      -2.072   5.943  25.185  1.00 12.49       A    N
ANISOU 1117  N   LYS A 488     1582   1418   1746    -26     65    -46  A    N
ATOM   1119  CA  LYS A 488      -3.478   6.269  25.322  1.00 13.72       A    C
ANISOU 1119  CA  LYS A 488     1732   1573   1909     79    -44      1  A    C
ATOM   1121  CB  LYS A 488      -3.880   6.171  26.785  1.00 15.01       A    C
ANISOU 1121  CB  LYS A 488     1939   1768   1996     75     24     33  A    C
ATOM   1124  CG  LYS A 488      -5.340   6.581  27.022  1.00 18.79       A    C
ANISOU 1124  CG  LYS A 488     2195   2347   2597    114      4    -67  A    C
ATOM   1127  CD  LYS A 488      -5.926   6.040  28.301  1.00 23.36       A    C
ANISOU 1127  CD  LYS A 488     2996   2977   2899     21     56     52  A    C
ATOM   1130  CE  LYS A 488      -7.455   5.893  28.165  1.00 25.89       A    C
ANISOU 1130  CE  LYS A 488     3144   3344   3348     -9    -37     28  A    C
ATOM   1133  NZ  LYS A 488      -8.211   5.808  29.464  1.00 28.78       A    N
ANISOU 1133  NZ  LYS A 488     3710   3660   3562    -17     28     36  A    N
ATOM   1137  C   LYS A 488      -3.791   7.673  24.817  1.00 13.81       A    C
ANISOU 1137  C   LYS A 488     1813   1503   1930      7     -9     14  A    C
ATOM   1138  O   LYS A 488      -3.234   8.669  25.327  1.00 13.74       A    O
ANISOU 1138  O   LYS A 488     1789   1333   2096    139   -142     39  A    O
ATOM   1139  N   LEU A 489      -4.670   7.723  23.826  1.00 14.99       A    N
ANISOU 1139  N   LEU A 489     1997   1595   2104     30    -56     15  A    N
ATOM   1141  CA  LEU A 489      -5.218   8.979  23.296  1.00 16.61       A    C
ANISOU 1141  CA  LEU A 489     2161   1908   2241     28    -64     42  A    C
ATOM   1143  CB  LEU A 489      -5.445   8.889  21.783  1.00 17.93       A    C
ANISOU 1143  CB  LEU A 489     2381   2080   2351     27    -59      0  A    C
ATOM   1146  CG  LEU A 489      -5.759  10.211  21.078  1.00 20.73       A    C
ANISOU 1146  CG  LEU A 489     2798   2384   2693    -42    -23     37  A    C
ATOM   1148  CD1 LEU A 489      -5.312  10.130  19.618  1.00 22.63       A    C
ANISOU 1148  CD1 LEU A 489     3054   2730   2815     -2    -45     33  A    C
ATOM   1152  CD2 LEU A 489      -7.204  10.543  21.212  1.00 22.83       A    C
ANISOU 1152  CD2 LEU A 489     2960   2703   3009     26   -126    -37  A    C
ATOM   1156  C   LEU A 489      -6.493   9.234  24.039  1.00 17.27       A    C
ANISOU 1156  C   LEU A 489     2161   2012   2386      0    -56     53  A    C
ATOM   1157  O   LEU A 489      -7.442   8.439  23.953  1.00 19.13       A    O
ANISOU 1157  O   LEU A 489     2297   2041   2930    -29    -52     68  A    O
ATOM   1158  N   ILE A 490      -6.531  10.339  24.781  1.00 16.86       A    N
ANISOU 1158  N   ILE A 490     2071   2069   2263     27     24     26  A    N
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ATOM   1160  CA  ILE A 490      -7.653  10.645  25.665  1.00 17.31           A    C
ANISOU 1160  CA  ILE A 490     2134   2134   2309     45     31     79  A    C
ATOM   1162  CB  ILE A 490      -7.153  11.481  26.830  1.00 17.50           A    C
ANISOU 1162  CB  ILE A 490     2191   2209   2249     42     30     61  A    C
ATOM   1164  CG1 ILE A 490      -6.191  10.662  27.693  1.00 18.79           A    C
ANISOU 1164  CG1 ILE A 490     2337   2365   2434     67      5      0  A    C
ATOM   1167  CD1 ILE A 490      -5.432  11.484  28.687  1.00 19.29           A    C
ANISOU 1167  CD1 ILE A 490     2445   2407   2475     17    -16    -56  A    C
ATOM   1171  CG2 ILE A 490      -8.330  12.031  27.654  1.00 18.76           A    C
ANISOU 1171  CG2 ILE A 490     2345   2390   2393     60     85     70  A    C
ATOM   1175  C   ILE A 490      -8.776  11.372  24.940  1.00 17.33           A    C
ANISOU 1175  C   ILE A 490     2102   2220   2260      3     13     97  A    C
ATOM   1176  O   ILE A 490      -9.951  11.089  25.159  1.00 18.68           A    O
ANISOU 1176  O   ILE A 490     2110   2361   2626     -4    -61    139  A    O
ATOM   1177  N   GLY A 491      -8.427  12.324  24.091  1.00 16.24           A    N
ANISOU 1177  N   GLY A 491     1928   2002   2238     21     -3     88  A    N
ATOM   1179  CA  GLY A 491      -9.453  13.017  23.337  1.00 16.22           A    C
ANISOU 1179  CA  GLY A 491     1991   2001   2171     19    -27     25  A    C
ATOM   1182  C   GLY A 491      -8.931  13.872  22.220  1.00 15.56           A    C
ANISOU 1182  C   GLY A 491     1888   1933   2092     -8    -28     20  A    C
ATOM   1183  O   GLY A 491      -7.740  14.041  22.046  1.00 14.32           A    O
ANISOU 1183  O   GLY A 491     1639   1560   2241    -21    -88     10  A    O
ATOM   1184  N   ILE A 492      -9.855  14.381  21.419  1.00 16.14           A    N
ANISOU 1184  N   ILE A 492     1926   1975   2229     19    -48     39  A    N
ATOM   1186  CA  ILE A 492      -9.532  15.195  20.260  1.00 17.06           A    C
ANISOU 1186  CA  ILE A 492     2088   2137   2255      3    -25     21  A    C
ATOM   1188  CB  ILE A 492      -9.742  14.397  18.950  1.00 17.37           A    C
ANISOU 1188  CB  ILE A 492     2124   2210   2264      6    -30     12  A    C
ATOM   1190  CG1 ILE A 492      -8.852  13.150  18.902  1.00 18.95           A    C
ANISOU 1190  CG1 ILE A 492     2443   2336   2420     57      4    -46  A    C
ATOM   1193  CD1 ILE A 492      -9.244  12.169  17.797  1.00 20.06           A    C
ANISOU 1193  CD1 ILE A 492     2623   2503   2495    -61    -65      6  A    C
ATOM   1197  CG2 ILE A 492      -9.469  15.274  17.749  1.00 19.11           A    C
ANISOU 1197  CG2 ILE A 492     2483   2378   2399    -31    -24     42  A    C
ATOM   1201  C   ILE A 492     -10.463  16.415  20.310  1.00 17.29           A    C
ANISOU 1201  C   ILE A 492     2054   2160   2356     26    -25     52  A    C
ATOM   1202  O   ILE A 492     -11.686  16.280  20.428  1.00 17.49           A    O
ANISOU 1202  O   ILE A 492     2030   2126   2486   -106    -25    125  A    O
ATOM   1203  N   ILE A 493      -9.882  17.607  20.268  1.00 16.77           A    N
ANISOU 1203  N   ILE A 493     2017   2032   2322     89    -22     63  A    N
ATOM   1205  CA  ILE A 493     -10.655  18.827  20.046  1.00 17.71           A    C
ANISOU 1205  CA  ILE A 493     2216   2141   2370     80    -43     47  A    C
ATOM   1207  CB  ILE A 493     -10.193  19.940  20.958  1.00 17.74           A    C
ANISOU 1207  CB  ILE A 493     2203   2198   2339    118    -25     46  A    C
ATOM   1209  CG1 ILE A 493     -10.306  19.495  22.415  1.00 19.40           A    C
ANISOU 1209  CG1 ILE A 493     2449   2457   2464     75    -11     52  A    C
ATOM   1212  CD1 ILE A 493      -9.703  20.456  23.344  1.00 21.40           A    C
ANISOU 1212  CD1 ILE A 493     2677   2726   2726     -3    -36    -32  A    C
ATOM   1216  CG2 ILE A 493     -11.022  21.222  20.690  1.00 17.23           A    C
ANISOU 1216  CG2 ILE A 493     2206   2039   2300     95     -5     63  A    C
ATOM   1220  C   ILE A 493     -10.395  19.163  18.603  1.00 18.30           A    C
ANISOU 1220  C   ILE A 493     2336   2214   2402     80    -27     31  A    C
ATOM   1221  O   ILE A 493      -9.308  19.592  18.238  1.00 17.19           A    O
ANISOU 1221  O   ILE A 493     2246   1979   2305    160   -159      3  A    O
ATOM   1222  N   GLU A 494     -11.418  18.985  17.779  1.00 20.26           A    N
ANISOU 1222  N   GLU A 494     2566   2512   2619     10    -82     -4  A    N
ATOM   1224  CA  GLU A 494     -11.262  19.089  16.330  1.00 22.00           A    C
ANISOU 1224  CA  GLU A 494     2798   2788   2770     23    -21     20  A    C
ATOM   1226  CB  GLU A 494     -12.443  18.395  15.635  1.00 22.98           A    C
ANISOU 1226  CB  GLU A 494     2893   2940   2896    -10    -54    -33  A    C
ATOM   1229  CG  GLU A 494     -12.641  16.927  16.006  1.00 25.89           A    C
ANISOU 1229  CG  GLU A 494     3352   3198   3284     14     -5     62  A    C
ATOM   1232  CD  GLU A 494     -13.947  16.341  15.472  1.00 30.25           A    C
ANISOU 1232  CD  GLU A 494     3768   3834   3891   -107    -67    -25  A    C
ATOM   1233  OE1 GLU A 494     -14.323  15.221  15.903  1.00 32.64           A    O
ANISOU 1233  OE1 GLU A 494     4256   3953   4191   -107    -14     33  A    O
ATOM   1234  OE2 GLU A 494     -14.608  16.997  14.628  1.00 32.77           A    O
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ANISOU 1234  OE2 GLU A 494     4137   4180   4133    -15   -110     61  A    O
ATOM   1235  C   GLU A 494    -11.165  20.550  15.875  1.00 22.26      A    C
ANISOU 1235  C   GLU A 494     2829   2822   2804      5    -17     12  A    C
ATOM   1236  O   GLU A 494    -10.408  20.881  14.955  1.00 22.49      A    O
ANISOU 1236  O   GLU A 494     2881   2892   2771     -2    -34     46  A    O
ATOM   1237  N   GLU A 495    -11.892  21.421  16.566  1.00 22.55      A    N
ANISOU 1237  N   GLU A 495     2859   2872   2834     32    -48     20  A    N
ATOM   1239  CA  GLU A 495    -12.028  22.821  16.164  1.00 23.10      A    C
ANISOU 1239  CA  GLU A 495     2913   2910   2953      8    -26     -1  A    C
ATOM   1241  CB  GLU A 495    -13.047  23.513  17.070  1.00 23.74      A    C
ANISOU 1241  CB  GLU A 495     3047   2983   2991     41    -17     -6  A    C
ATOM   1244  CG  GLU A 495    -14.487  23.077  16.818  1.00 25.77      A    C
ANISOU 1244  CG  GLU A 495     3199   3311   3280    -10    -24    -23  A    C
ATOM   1247  CD  GLU A 495    -14.984  21.935  17.706  1.00 28.15      A    C
ANISOU 1247  CD  GLU A 495     3598   3530   3567     -3      8     87  A    C
ATOM   1248  OE1 GLU A 495    -14.178  21.250  18.372  1.00 28.67      A    O
ANISOU 1248  OE1 GLU A 495     3561   3664   3666     86     -2     42  A    O
ATOM   1249  OE2 GLU A 495    -16.216  21.716  17.746  1.00 30.21      A    O
ANISOU 1249  OE2 GLU A 495     3742   3840   3896    -40    -35     22  A    O
ATOM   1250  C   GLU A 495    -10.688  23.549  16.206  1.00 22.54      A    C
ANISOU 1250  C   GLU A 495     2852   2842   2869     26    -20    -60  A    C
ATOM   1251  O   GLU A 495     -9.768  23.126  16.933  1.00 21.30      A    O
ANISOU 1251  O   GLU A 495     2746   2563   2784     -7    -38     27  A    O
ATOM   1252  N   GLU A 496    -10.998  25.197  16.115  0.00 27.68      A    N
ANISOU 1252  N   GLU A 496     3506   3506   3506      0      0      0  A    N
ATOM   1254  CA  GLU A 496     -9.609  27.027  16.947  1.00 19.02      A    C
ANISOU 1254  CA  GLU A 496     2418   2426   2383    -10     -8     41  A    C
ATOM   1256  CB  GLU A 496    -10.924  26.542  17.542  1.00 20.20      A    C
ANISOU 1256  CB  GLU A 496     2589   2557   2526    -73      0     58  A    C
ATOM   1259  CG  GLU A 496    -11.154  28.033  17.552  0.00 24.82      A    C
ANISOU 1259  CG  GLU A 496     3143   3143   3143      0      0      0  A    C
ATOM   1262  CD  GLU A 496    -11.168  28.880  18.814  0.00 24.31      A    C
ANISOU 1262  CD  GLU A 496     3079   3079   3079      0      0      0  A    C
ATOM   1263  OE1 GLU A 496    -10.146  29.543  19.101  0.00 24.05      A    O
ANISOU 1263  OE1 GLU A 496     3046   3046   3046      0      0      0  A    O
ATOM   1264  OE2 GLU A 496    -12.203  28.889  19.513  0.00 24.05      A    O
ANISOU 1264  OE2 GLU A 496     3046   3046   3046      0      0      0  A    O
ATOM   1265  C   GLU A 496     -8.667  25.895  16.623  1.00 18.59      A    C
ANISOU 1265  C   GLU A 496     2385   2359   2317    -46    -12     65  A    C
ATOM   1266  O   GLU A 496     -8.359  24.644  15.324  0.00 25.40      A    O
ANISOU 1266  O   GLU A 496     3217   3217   3217      0      0      0  A    O
ATOM   1267  N   PRO A 497     -7.493  25.950  17.245  1.00 17.85      A    N
ANISOU 1267  N   PRO A 497     2297   2252   2230    -14     14     39  A    N
ATOM   1268  CA  PRO A 497     -6.400  25.047  16.901  1.00 17.30      A    C
ANISOU 1268  CA  PRO A 497     2270   2149   2152    -10     -1     39  A    C
ATOM   1270  CB  PRO A 497     -5.211  25.617  17.674  1.00 17.74      A    C
ANISOU 1270  CB  PRO A 497     2272   2241   2225    -16     -1     22  A    C
ATOM   1273  CG  PRO A 497     -5.805  26.406  18.785  1.00 18.13      A    C
ANISOU 1273  CG  PRO A 497     2355   2309   2225     -8      5     28  A    C
ATOM   1276  CD  PRO A 497     -7.131  26.875  18.331  1.00 17.50      A    C
ANISOU 1276  CD  PRO A 497     2265   2174   2209      3     28      8  A    C
ATOM   1279  C   PRO A 497     -6.718  23.634  17.364  1.00 16.79      A    C
ANISOU 1279  C   PRO A 497     2219   2066   2094      0     11     -7  A    C
ATOM   1280  O   PRO A 497     -7.105  23.424  18.502  1.00 15.67      A    O
ANISOU 1280  O   PRO A 497     2139   1856   1957     -7     -7     51  A    O
ATOM   1281  N   THR A 498     -6.574  22.689  16.454  1.00 16.24      A    N
ANISOU 1281  N   THR A 498     2193   1995   1979    -10    -12     10  A    N
ATOM   1283  CA  THR A 498     -6.826  21.298  16.743  1.00 16.32      A    C
ANISOU 1283  CA  THR A 498     2150   2031   2018     15    -10    -22  A    C
ATOM   1285  CB  THR A 498     -6.645  20.528  15.461  1.00 17.01      A    C
ANISOU 1285  CB  THR A 498     2249   2118   2095     11     -7    -62  A    C
ATOM   1287  OG1 THR A 498     -7.585  21.017  14.504  1.00 19.42      A    O
ANISOU 1287  OG1 THR A 498     2556   2625   2195     -5    -72   -128  A    O
ATOM   1289  CG2 THR A 498     -6.987  19.070  15.648  1.00 18.09      A    C
ANISOU 1289  CG2 THR A 498     2409   2207   2254    -39    -60     30  A    C
ATOM   1293  C   THR A 498     -5.873  20.796  17.805  1.00 14.82      A    C
ANISOU 1293  C   THR A 498     1955   1828   1845    -15     12    -22  A    C
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ATOM   1294  O   THR A 498      -4.679  21.065  17.728  1.00 14.45           A    O
ANISOU 1294  O   THR A 498     1997   1650   1840      9     25    -11  A    O
ATOM   1295  N   TRP A 499      -6.413  20.095  18.808  1.00 13.64           A    N
ANISOU 1295  N   TRP A 499     1766   1645   1770     29    -52     20  A    N
ATOM   1297  CA  TRP A 499      -5.611  19.466  19.852  1.00 12.85           A    C
ANISOU 1297  CA  TRP A 499     1698   1530   1654    -31    -45     49  A    C
ATOM   1299  CB  TRP A 499      -5.999  19.998  21.227  1.00 11.89           A    C
ANISOU 1299  CB  TRP A 499     1551   1359   1605     46    -27     74  A    C
ATOM   1302  CG  TRP A 499      -5.594  21.411  21.543  1.00 10.80           A    C
ANISOU 1302  CG  TRP A 499     1448   1361   1293    -34    -35     59  A    C
ATOM   1303  CD1 TRP A 499      -4.952  22.301  20.725  1.00 11.96           A    C
ANISOU 1303  CD1 TRP A 499     1697   1428   1417   -126     10    -19  A    C
ATOM   1305  NE1 TRP A 499      -4.758  23.486  21.386  1.00 10.80           A    N
ANISOU 1305  NE1 TRP A 499     1627   1194   1281     16     -6     65  A    N
ATOM   1307  CE2 TRP A 499      -5.270  23.389  22.647  1.00 11.62           A    C
ANISOU 1307  CE2 TRP A 499     1482   1456   1476     51     -4     68  A    C
ATOM   1308  CD2 TRP A 499      -5.812  22.098  22.778  1.00  9.92           A    C
ANISOU 1308  CD2 TRP A 499     1272   1276   1218     43      8     18  A    C
ATOM   1309  CE3 TRP A 499      -6.398  21.739  24.006  1.00 11.26           A    C
ANISOU 1309  CE3 TRP A 499     1373   1445   1459      0      8    191  A    C
ATOM   1311  CZ3 TRP A 499      -6.425  22.666  25.022  1.00 12.18           A    C
ANISOU 1311  CZ3 TRP A 499     1618   1691   1316     27     25    183  A    C
ATOM   1313  CH2 TRP A 499      -5.902  23.958  24.858  1.00 13.93           A    C
ANISOU 1313  CH2 TRP A 499     1773   1878   1639    -84     65     20  A    C
ATOM   1315  CZ2 TRP A 499      -5.317  24.341  23.677  1.00 12.47           A    C
ANISOU 1315  CZ2 TRP A 499     1647   1680   1409    -67    -25     32  A    C
ATOM   1317  C   TRP A 499      -5.854  17.966  19.870  1.00 12.90           A    C
ANISOU 1317  C   TRP A 499     1673   1527   1700      1    -22      2  A    C
ATOM   1318  O   TRP A 499      -7.015  17.536  19.903  1.00 14.17           A    O
ANISOU 1318  O   TRP A 499     1881   1504   1997    -34    -74     72  A    O
ATOM   1319  N   ILE A 500      -4.768  17.194  19.886  1.00 11.88           A    N
ANISOU 1319  N   ILE A 500     1587   1390   1535     -1    -37     46  A    N
ATOM   1321  CA  ILE A 500      -4.824  15.769  20.179  1.00 12.14           A    C
ANISOU 1321  CA  ILE A 500     1573   1451   1589    -38    -40     21  A    C
ATOM   1323  CB  ILE A 500      -4.030  14.965  19.133  1.00 13.42           A    C
ANISOU 1323  CB  ILE A 500     1744   1624   1731    -13      0     21  A    C
ATOM   1325  CG1 ILE A 500      -4.536  15.253  17.713  1.00 16.00           A    C
ANISOU 1325  CG1 ILE A 500     2127   1977   1973      7    -56     80  A    C
ATOM   1328  CD1 ILE A 500      -6.012  15.212  17.531  1.00 18.88           A    C
ANISOU 1328  CD1 ILE A 500     2343   2457   2372     15     16     10  A    C
ATOM   1332  CG2 ILE A 500      -4.094  13.472  19.419  1.00 14.86           A    C
ANISOU 1332  CG2 ILE A 500     2003   1694   1946    -68    -63    -14  A    C
ATOM   1336  C   ILE A 500      -4.273  15.587  21.582  1.00 11.17           A    C
ANISOU 1336  C   ILE A 500     1417   1310   1515    -44    -42      1  A    C
ATOM   1337  O   ILE A 500      -3.112  15.868  21.867  1.00 11.84           A    O
ANISOU 1337  O   ILE A 500     1452   1347   1699   -110    -65     43  A    O
ATOM   1338  N   ILE A 501      -5.129  15.142  22.476  1.00 10.69           A    N
ANISOU 1338  N   ILE A 501     1402   1215   1443    -11    -47     16  A    N
ATOM   1340  CA  ILE A 501      -4.804  15.065  23.883  1.00 10.07           A    C
ANISOU 1340  CA  ILE A 501     1289   1167   1371    -33    -41     -1  A    C
ATOM   1342  CB  ILE A 501      -6.002  15.548  24.757  1.00 10.35           A    C
ANISOU 1342  CB  ILE A 501     1289   1232   1409    -19    -22     10  A    C
ATOM   1344  CG1 ILE A 501      -6.453  16.956  24.336  1.00 11.96           A    C
ANISOU 1344  CG1 ILE A 501     1570   1393   1580    -13    -59     22  A    C
ATOM   1347  CD1 ILE A 501      -7.847  17.192  24.617  1.00 13.84           A    C
ANISOU 1347  CD1 ILE A 501     1751   1603   1904     63    -39      6  A    C
ATOM   1351  CG2 ILE A 501      -5.657  15.564  26.216  1.00  9.55           A    C
ANISOU 1351  CG2 ILE A 501     1196   1033   1397     99     36    -76  A    C
ATOM   1355  C   ILE A 501      -4.426  13.624  24.187  1.00 10.31           A    C
ANISOU 1355  C   ILE A 501     1320   1158   1437    -38    -41     16  A    C
ATOM   1356  O   ILE A 501      -5.255  12.719  24.059  1.00 10.06           A    O
ANISOU 1356  O   ILE A 501     1331   1022   1467    -98     15     16  A    O
ATOM   1357  N   MET A 502      -3.167  13.435  24.568  1.00 10.54           A    N
ANISOU 1357  N   MET A 502     1331   1201   1471     -4     -2     32  A    N
ATOM   1359  CA  MET A 502      -2.621  12.134  24.964  1.00 11.99           A    C
ANISOU 1359  CA  MET A 502     1590   1341   1622     21    -10     -7  A    C
ATOM   1361  CB  MET A 502      -1.303  11.888  24.242  1.00 13.19           A    C
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ANISOU 1361  CB  MET A 502     1721   1540   1750     37     41     38  A    C
ATOM   1364  CG  MET A 502      -1.346  11.998  22.722  1.00 17.72        A    C
ANISOU 1364  CG  MET A 502     2343   2292   2098     42    -40     50  A    C
ATOM   1367  SD  MET A 502      -2.388  10.754  21.972  1.00 20.40        A    S
ANISOU 1367  SD  MET A 502     2893   2505   2353     65   -156    -87  A    S
ATOM   1368  CE  MET A 502      -1.484   9.269  22.260  1.00 21.03        A    C
ANISOU 1368  CE  MET A 502     2677   2560   2750     24    -24    -11  A    C
ATOM   1372  C   MET A 502      -2.324  12.079  26.447  1.00 11.47        A    C
ANISOU 1372  C   MET A 502     1448   1318   1590     59      7    -13  A    C
ATOM   1373  O   MET A 502      -2.052  13.086  27.078  1.00 10.71        A    O
ANISOU 1373  O   MET A 502     1324   1276   1467     40     46   -165  A    O
ATOM   1374  N   GLU A 503      -2.325  10.884  27.007  1.00 11.37        A    N
ANISOU 1374  N   GLU A 503     1479   1262   1578     38     21    -36  A    N
ATOM   1376  CA  GLU A 503      -1.693  10.661  28.304  1.00 13.03        A    C
ANISOU 1376  CA  GLU A 503     1642   1622   1684     59     -6    -29  A    C
ATOM   1378  CB  GLU A 503      -1.809   9.175  28.658  1.00 14.57        A    C
ANISOU 1378  CB  GLU A 503     1822   1742   1972     -3    -12    -11  A    C
ATOM   1381  CG  GLU A 503      -1.514   8.790  30.099  1.00 19.60        A    C
ANISOU 1381  CG  GLU A 503     2498   2570   2377      2    -70     56  A    C
ATOM   1384  CD  GLU A 503      -1.930   7.350  30.408  1.00 23.91        A    C
ANISOU 1384  CD  GLU A 503     3150   2793   3142     -3    -26     83  A    C
ATOM   1385  OE1 GLU A 503      -1.691   6.447  29.580  1.00 27.71        A    O
ANISOU 1385  OE1 GLU A 503     3785   3287   3455    -78   -100    -74  A    O
ATOM   1386  OE2 GLU A 503      -2.491   7.109  31.485  1.00 28.61        A    O
ANISOU 1386  OE2 GLU A 503     3684   3605   3578    -13    127     58  A    O
ATOM   1387  C   GLU A 503      -0.220  11.115  28.273  1.00 13.12        A    C
ANISOU 1387  C   GLU A 503     1637   1676   1670     61    -22    -28  A    C
ATOM   1388  O   GLU A 503       0.480  10.902  27.277  1.00 14.04        A    O
ANISOU 1388  O   GLU A 503     1672   1832   1830    179    -63    -63  A    O
ATOM   1389  N   LEU A 504       0.225  11.793  29.338  1.00 12.78        A    N
ANISOU 1389  N   LEU A 504     1560   1617   1679    107    -26    -59  A    N
ATOM   1391  CA  LEU A 504       1.621  12.220  29.470  1.00 13.70        A    C
ANISOU 1391  CA  LEU A 504     1729   1724   1751     55    -17      0  A    C
ATOM   1393  CB  LEU A 504       1.723  13.411  30.433  1.00 13.89        A    C
ANISOU 1393  CB  LEU A 504     1753   1720   1804    101    -35    -24  A    C
ATOM   1396  CG  LEU A 504       3.133  13.978  30.629  1.00 15.44        A    C
ANISOU 1396  CG  LEU A 504     1938   1908   2020     14    -12    -49  A    C
ATOM   1398  CD1 LEU A 504       3.589  14.615  29.325  1.00 17.03        A    C
ANISOU 1398  CD1 LEU A 504     2149   2227   2094    -11     25     24  A    C
ATOM   1402  CD2 LEU A 504       3.177  14.991  31.799  1.00 16.68        A    C
ANISOU 1402  CD2 LEU A 504     2189   1996   2152     -5     21    -80  A    C
ATOM   1406  C   LEU A 504       2.447  11.061  30.018  1.00 14.74        A    C
ANISOU 1406  C   LEU A 504     1804   1920   1874     53    -50     56  A    C
ATOM   1407  O   LEU A 504       2.068  10.438  31.003  1.00 15.36        A    O
ANISOU 1407  O   LEU A 504     1757   2086   1992    189      6    211  A    O
ATOM   1408  N   TYR A 505       3.566  10.793  29.363  1.00 15.03        A    N
ANISOU 1408  N   TYR A 505     1874   1945   1889    159    -46     44  A    N
ATOM   1410  CA  TYR A 505       4.542   9.782  29.780  1.00 16.40        A    C
ANISOU 1410  CA  TYR A 505     2080   2063   2087    135    -35     45  A    C
ATOM   1412  CB  TYR A 505       4.712   8.775  28.642  1.00 16.92        A    C
ANISOU 1412  CB  TYR A 505     2164   2116   2148    181    -22     14  A    C
ATOM   1415  CG  TYR A 505       3.387   8.093  28.346  1.00 18.81        A    C
ANISOU 1415  CG  TYR A 505     2304   2428   2414    158    -32     -7  A    C
ATOM   1416  CD1 TYR A 505       2.721   7.364  29.326  1.00 20.24        A    C
ANISOU 1416  CD1 TYR A 505     2509   2451   2728     97    -78    115  A    C
ATOM   1418  CE1 TYR A 505       1.484   6.776  29.075  1.00 21.60        A    C
ANISOU 1418  CE1 TYR A 505     2771   2650   2784      6   -144     53  A    C
ATOM   1420  CZ  TYR A 505       0.893   6.938  27.824  1.00 19.04        A    C
ANISOU 1420  CZ  TYR A 505     2563   2102   2568    192    -66    -18  A    C
ATOM   1421  OH  TYR A 505      -0.337   6.366  27.585  1.00 20.41        A    O
ANISOU 1421  OH  TYR A 505     2876   1975   2900    241   -198    -48  A    O
ATOM   1423  CE2 TYR A 505       1.528   7.670  26.856  1.00 19.06        A    C
ANISOU 1423  CE2 TYR A 505     2405   2382   2454    196    -26    -86  A    C
ATOM   1425  CD2 TYR A 505       2.746   8.264  27.121  1.00 19.86        A    C
ANISOU 1425  CD2 TYR A 505     2525   2624   2396    152      1   -144  A    C
ATOM   1427  C   TYR A 505       5.812  10.535  30.149  1.00 16.38        A    C
ANISOU 1427  C   TYR A 505     2097   2053   2074    197    -44     17  A    C
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ATOM   1428  O   TYR A 505       6.641  10.855  29.316  1.00 16.56           A    O
ANISOU 1428  O   TYR A 505    2150   1986   2155    248    -51     99  A    O
ATOM   1429  N   PRO A 506       5.924  10.899  31.420  1.00 17.54           A    N
ANISOU 1429  N   PRO A 506    2179   2305   2178    148    -26     35  A    N
ATOM   1430  CA  PRO A 506       6.936  11.865  31.844  1.00 17.08           A    C
ANISOU 1430  CA  PRO A 506    2193   2166   2131    118     10    -15  A    C
ATOM   1432  CB  PRO A 506       6.574  12.136  33.306  1.00 17.97           A    C
ANISOU 1432  CB  PRO A 506    2330   2327   2169     91     32     20  A    C
ATOM   1435  CG  PRO A 506       5.824  10.925  33.738  1.00 17.80           A    C
ANISOU 1435  CG  PRO A 506    2275   2259   2227     44      3   -115  A    C
ATOM   1438  CD  PRO A 506       5.110  10.381  32.534  1.00 17.74           A    C
ANISOU 1438  CD  PRO A 506    2230   2321   2187    100    -56     30  A    C
ATOM   1441  C   PRO A 506       8.384  11.346  31.734  1.00 16.27           A    C
ANISOU 1441  C   PRO A 506    2071   1999   2111     54     15    -32  A    C
ATOM   1442  O   PRO A 506       9.316  12.131  31.656  1.00 16.69           A    O
ANISOU 1442  O   PRO A 506    2253   1902   2185     47    -19    -77  A    O
ATOM   1443  N   TYR A 507       8.567  10.031  31.721  1.00 14.24           A    N
ANISOU 1443  N   TYR A 507    1798   1774   1838     46    -25    -65  A    N
ATOM   1445  CA  TYR A 507       9.904   9.477  31.587  1.00 12.77           A    C
ANISOU 1445  CA  TYR A 507    1591   1593   1668     10    -11    -38  A    C
ATOM   1447  CB  TYR A 507       9.964   8.074  32.166  1.00 12.48           A    C
ANISOU 1447  CB  TYR A 507    1465   1590   1687     25     25    -63  A    C
ATOM   1450  CG  TYR A 507       9.736   8.018  33.654  1.00 12.63           A    C
ANISOU 1450  CG  TYR A 507    1612   1485   1700     17    -50      1  A    C
ATOM   1451  CD1 TYR A 507      10.786   8.202  34.542  1.00 13.86           A    C
ANISOU 1451  CD1 TYR A 507    1656   1856   1754     42    -26   -110  A    C
ATOM   1453  CE1 TYR A 507      10.589   8.151  35.916  1.00 15.19           A    C
ANISOU 1453  CE1 TYR A 507    1910   2047   1812     28    -16    -35  A    C
ATOM   1455  CZ  TYR A 507       9.339   7.892  36.415  1.00 16.05           A    C
ANISOU 1455  CZ  TYR A 507    1938   2236   1923    -43     -3    -81  A    C
ATOM   1456  OH  TYR A 507       9.173   7.852  37.775  1.00 19.87           A    O
ANISOU 1456  OH  TYR A 507    2688   2691   2169    -70     -3    -15  A    O
ATOM   1458  CE2 TYR A 507       8.266   7.707  35.554  1.00 14.97           A    C
ANISOU 1458  CE2 TYR A 507    1915   1955   1818    -37     -5     46  A    C
ATOM   1460  CD2 TYR A 507       8.480   7.754  34.175  1.00 12.99           A    C
ANISOU 1460  CD2 TYR A 507    1623   1582   1731     60     24    -80  A    C
ATOM   1462  C   TYR A 507      10.395   9.481  30.148  1.00 11.87           A    C
ANISOU 1462  C   TYR A 507    1497   1402   1609     22    -49    -37  A    C
ATOM   1463  O   TYR A 507      11.570   9.211  29.900  1.00 12.76           A    O
ANISOU 1463  O   TYR A 507    1543   1492   1813    100     -1    -13  A    O
ATOM   1464  N   GLY A 508       9.517   9.776  29.187  1.00 11.45           A    N
ANISOU 1464  N   GLY A 508    1455   1342   1553     90    -23    -75  A    N
ATOM   1466  CA  GLY A 508       9.926   9.887  27.811  1.00 11.62           A    C
ANISOU 1466  CA  GLY A 508    1501   1371   1542     35    -41    -35  A    C
ATOM   1469  C   GLY A 508      10.173   8.594  27.050  1.00 11.14           A    C
ANISOU 1469  C   GLY A 508    1422   1325   1484     52     52    -20  A    C
ATOM   1470  O   GLY A 508       9.661   7.541  27.396  1.00 10.63           A    O
ANISOU 1470  O   GLY A 508    1361   1324   1351     48    121    -26  A    O
ATOM   1471  N   GLU A 509      10.939   8.721  25.967  1.00 10.48           A    N
ANISOU 1471  N   GLU A 509    1444   1200   1338     52     61    -37  A    N
ATOM   1473  CA  GLU A 509      11.240   7.585  25.103  1.00 11.08           A    C
ANISOU 1473  CA  GLU A 509    1457   1332   1420     44     -9    -59  A    C
ATOM   1475  CB  GLU A 509      11.999   8.040  23.875  1.00 11.95           A    C
ANISOU 1475  CB  GLU A 509    1574   1429   1536     22     27     -6  A    C
ATOM   1478  CG  GLU A 509      11.176   8.934  22.952  1.00 13.26           A    C
ANISOU 1478  CG  GLU A 509    1705   1599   1731    104    -17     34  A    C
ATOM   1481  CD  GLU A 509      11.969   9.497  21.781  1.00 16.05           A    C
ANISOU 1481  CD  GLU A 509    2080   2080   1937     21     59     45  A    C
ATOM   1482  OE1 GLU A 509      13.142   9.112  21.572  1.00 16.36           A    O
ANISOU 1482  OE1 GLU A 509    2205   1850   2158     63     18     99  A    O
ATOM   1483  OE2 GLU A 509      11.397  10.356  21.073  1.00 20.02           A    O
ANISOU 1483  OE2 GLU A 509    2779   2307   2520    164     27    169  A    O
ATOM   1484  C   GLU A 509      12.060   6.531  25.806  1.00 10.19           A    C
ANISOU 1484  C   GLU A 509    1312   1249   1308     -7    -26    -37  A    C
ATOM   1485  O   GLU A 509      12.972   6.850  26.552  1.00 11.22           A    O
ANISOU 1485  O   GLU A 509    1438   1460   1365    163   -105    -66  A    O
ATOM   1486  N   LEU A 510      11.781   5.273  25.494  1.00 10.30           A    N
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ANISOU 1486  N   LEU A 510     1356   1268   1288     57    -39    -60  A    N
ATOM   1488  CA  LEU A 510      12.486   4.176  26.098  1.00 10.07       A    C
ANISOU 1488  CA  LEU A 510     1303   1288   1235     11     14    -18  A    C
ATOM   1490  CB  LEU A 510      11.839   2.836  25.722  1.00 10.20       A    C
ANISOU 1490  CB  LEU A 510     1374   1251   1249    -11     72     -9  A    C
ATOM   1493  CG  LEU A 510      12.436   1.566  26.308  1.00  9.60       A    C
ANISOU 1493  CG  LEU A 510     1103   1347   1194     38     67    -38  A    C
ATOM   1495  CD1 LEU A 510      12.459   1.659  27.841  1.00  9.22       A    C
ANISOU 1495  CD1 LEU A 510     1211   1114   1175     88     55    -61  A    C
ATOM   1499  CD2 LEU A 510      11.682   0.370  25.821  1.00 10.25       A    C
ANISOU 1499  CD2 LEU A 510     1325   1204   1363     90    110    -80  A    C
ATOM   1503  C   LEU A 510      13.968   4.163  25.765  1.00  9.99       A    C
ANISOU 1503  C   LEU A 510     1312   1249   1235     22     49    -29  A    C
ATOM   1504  O   LEU A 510      14.760   3.823  26.632  1.00  9.82       A    O
ANISOU 1504  O   LEU A 510     1364   1174   1193     11     80    -97  A    O
ATOM   1505  N   GLY A 511      14.357   4.502  24.532  1.00 10.34       A    N
ANISOU 1505  N   GLY A 511     1267   1323   1335     -4     40    -52  A    N
ATOM   1507  CA  GLY A 511      15.773   4.432  24.191  1.00 10.19       A    C
ANISOU 1507  CA  GLY A 511     1240   1269   1359    -54     -1    -36  A    C
ATOM   1510  C   GLY A 511      16.598   5.311  25.121  1.00 10.62       A    C
ANISOU 1510  C   GLY A 511     1302   1345   1387    -21     -8    -10  A    C
ATOM   1511  O   GLY A 511      17.570   4.853  25.744  1.00 10.45       A    O
ANISOU 1511  O   GLY A 511     1160   1348   1460    -17     -4    -14  A    O
ATOM   1512  N   HIS A 512      16.194   6.563  25.238  1.00 10.65       A    N
ANISOU 1512  N   HIS A 512     1316   1418   1312    -22     -1    -29  A    N
ATOM   1514  CA  HIS A 512      16.915   7.499  26.076  1.00 11.18       A    C
ANISOU 1514  CA  HIS A 512     1376   1430   1442    -50    -39    -60  A    C
ATOM   1516  CB  HIS A 512      16.422   8.925  25.835  1.00 12.25       A    C
ANISOU 1516  CB  HIS A 512     1527   1468   1657    -15    -28    -80  A    C
ATOM   1519  CG  HIS A 512      16.638   9.391  24.428  1.00 17.53       A    C
ANISOU 1519  CG  HIS A 512     2421   2148   2089   -185     -8     -1  A    C
ATOM   1520  ND1 HIS A 512      16.129  10.570  23.938  1.00 24.90       A    N
ANISOU 1520  ND1 HIS A 512     3433   2964   3063    182     39    146  A    N
ATOM   1522  CE1 HIS A 512      16.471  10.709  22.668  1.00 24.85       A    C
ANISOU 1522  CE1 HIS A 512     3320   3104   3017     91     17     46  A    C
ATOM   1524  NE2 HIS A 512      17.154   9.644  22.303  1.00 24.72       A    N
ANISOU 1524  NE2 HIS A 512     3427   2884   3081    -99    130    124  A    N
ATOM   1526  CD2 HIS A 512      17.266   8.800  23.384  1.00 23.85       A    C
ANISOU 1526  CD2 HIS A 512     3241   2958   2863    175    153    -11  A    C
ATOM   1528  C   HIS A 512      16.830   7.106  27.555  1.00 10.37       A    C
ANISOU 1528  C   HIS A 512     1271   1317   1350    -53     29    -64  A    C
ATOM   1529  O   HIS A 512      17.811   7.238  28.288  1.00 10.94       A    O
ANISOU 1529  O   HIS A 512     1404   1252   1500    -17      0   -185  A    O
ATOM   1530  N   TYR A 513      15.683   6.581  27.978  1.00  9.37       A    N
ANISOU 1530  N   TYR A 513     1234   1083   1240     37     36    -82  A    N
ATOM   1532  CA  TYR A 513      15.521   6.095  29.335  1.00  9.93       A    C
ANISOU 1532  CA  TYR A 513     1269   1297   1206     32     30    -86  A    C
ATOM   1534  CB  TYR A 513      14.094   5.612  29.532  1.00  9.27       A    C
ANISOU 1534  CB  TYR A 513     1215   1221   1084     43     63    -47  A    C
ATOM   1537  CG  TYR A 513      13.766   5.046  30.887  1.00  8.67       A    C
ANISOU 1537  CG  TYR A 513     1183   1067   1044     65    117    -28  A    C
ATOM   1538  CD1 TYR A 513      13.205   5.856  31.881  1.00  9.29       A    C
ANISOU 1538  CD1 TYR A 513     1235   1104   1191    -58     12   -129  A    C
ATOM   1540  CE1 TYR A 513      12.882   5.336  33.110  1.00 10.43       A    C
ANISOU 1540  CE1 TYR A 513     1344   1343   1275     -3    -28   -115  A    C
ATOM   1542  CZ  TYR A 513      13.064   4.002  33.362  1.00 10.54       A    C
ANISOU 1542  CZ  TYR A 513     1127   1426   1449    -42     28     66  A    C
ATOM   1543  OH  TYR A 513      12.721   3.521  34.590  1.00 11.85       A    O
ANISOU 1543  OH  TYR A 513     1458   1688   1356    -15    115    -81  A    O
ATOM   1545  CE2 TYR A 513      13.616   3.167  32.409  1.00 10.42       A    C
ANISOU 1545  CE2 TYR A 513     1323   1221   1415   -124     61     61  A    C
ATOM   1547  CD2 TYR A 513      13.946   3.690  31.158  1.00 11.11       A    C
ANISOU 1547  CD2 TYR A 513     1515   1370   1334    137    111     53  A    C
ATOM   1549  C   TYR A 513      16.518   4.970  29.634  1.00  9.64       A    C
ANISOU 1549  C   TYR A 513     1285   1214   1162     56     -8    -54  A    C
ATOM   1550  O   TYR A 513      17.173   4.985  30.673  1.00  9.60       A    O
ANISOU 1550  O   TYR A 513     1340   1279   1028     69     69    -97  A    O
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ATOM	1551	N	LEU	A	514	16.675	4.010	28.717	1.00	9.19			A		N
ANISOU	1551	N	LEU	A	514	1287	1254	951	27	-69	-75	A	N		
ATOM	1553	CA	LEU	A	514	17.637	2.925	28.906	1.00	9.98			A		C
ANISOU	1553	CA	LEU	A	514	1279	1317	1195	18	43	-75	A	C		
ATOM	1555	CB	LEU	A	514	17.524	1.887	27.779	1.00	10.88			A		C
ANISOU	1555	CB	LEU	A	514	1389	1325	1417	74	37	-134	A	C		
ATOM	1558	CG	LEU	A	514	16.189	1.150	27.715	1.00	11.46			A		C
ANISOU	1558	CG	LEU	A	514	1449	1429	1476	56	37	-113	A	C		
ATOM	1560	CD1	LEU	A	514	16.101	0.400	26.403	1.00	13.32			A		C
ANISOU	1560	CD1	LEU	A	514	1685	1796	1579	34	-17	-191	A	C		
ATOM	1564	CD2	LEU	A	514	16.002	0.211	28.866	1.00	13.98			A		C
ANISOU	1564	CD2	LEU	A	514	1802	1662	1848	-10	-52	33	A	C		
ATOM	1568	C	LEU	A	514	19.068	3.440	29.001	1.00	10.78			A		C
ANISOU	1568	C	LEU	A	514	1372	1373	1350	44	17	-91	A	C		
ATOM	1569	O	LEU	A	514	19.854	2.962	29.807	1.00	10.98			A		O
ANISOU	1569	O	LEU	A	514	1302	1545	1323	38	33	-120	A	O		
ATOM	1570	N	GLU	A	515	19.393	4.405	28.162	1.00	11.53			A		N
ANISOU	1570	N	GLU	A	515	1466	1504	1409	18	52	-33	A	N		
ATOM	1572	CA	GLU	A	515	20.722	5.000	28.158	1.00	13.11			A		C
ANISOU	1572	CA	GLU	A	515	1605	1704	1672	-13	-9	-45	A	C		
ATOM	1574	CB	GLU	A	515	20.810	6.059	27.065	1.00	14.02			A		C
ANISOU	1574	CB	GLU	A	515	1652	1837	1837	-26	16	32	A	C		
ATOM	1577	CG	GLU	A	515	20.845	5.572	25.630	1.00	17.06			A		C
ANISOU	1577	CG	GLU	A	515	2083	2245	2154	-72	7	-89	A	C		
ATOM	1580	CD	GLU	A	515	20.592	6.709	24.629	1.00	21.59			A		C
ANISOU	1580	CD	GLU	A	515	2890	2657	2654	-41	-32	123	A	C		
ATOM	1581	OE1	GLU	A	515	20.608	7.895	25.042	1.00	27.20			A		O
ANISOU	1581	OE1	GLU	A	515	3781	3229	3325	69	29	-96	A	O		
ATOM	1582	OE2	GLU	A	515	20.384	6.444	23.418	1.00	24.09			A		O
ANISOU	1582	OE2	GLU	A	515	3216	3100	2834	12	-27	-6	A	O		
ATOM	1583	C	GLU	A	515	21.037	5.637	29.521	1.00	13.80			A		C
ANISOU	1583	C	GLU	A	515	1732	1775	1734	-43	-47	-10	A	C		
ATOM	1584	O	GLU	A	515	22.100	5.366	30.096	1.00	15.50			A		O
ANISOU	1584	O	GLU	A	515	1837	2077	1972	-22	-48	-3	A	O		
ATOM	1585	N	ARG	A	516	20.106	6.452	30.027	1.00	13.54			A		N
ANISOU	1585	N	ARG	A	516	1705	1782	1656	-18	-88	-56	A	N		
ATOM	1587	CA	ARG	A	516	20.250	7.179	31.311	1.00	14.19			A		C
ANISOU	1587	CA	ARG	A	516	1795	1863	1730	-5	-61	-64	A	C		
ATOM	1589	CB	ARG	A	516	18.972	7.991	31.640	1.00	15.29			A		C
ANISOU	1589	CB	ARG	A	516	2017	1903	1889	37	-24	-67	A	C		
ATOM	1592	CG	ARG	A	516	18.762	9.181	30.826	1.00	17.75			A		C
ANISOU	1592	CG	ARG	A	516	2275	2241	2228	44	-47	12	A	C		
ATOM	1595	CD	ARG	A	516	17.877	10.195	31.461	1.00	17.62			A		C
ANISOU	1595	CD	ARG	A	516	2249	2185	2259	-5	81	-18	A	C		
ATOM	1598	NE	ARG	A	516	16.507	9.747	31.733	1.00	15.87			A		N
ANISOU	1598	NE	ARG	A	516	2097	1890	2040	13	34	-130	A	N		
ATOM	1600	CZ	ARG	A	516	15.551	9.616	30.834	1.00	15.53			A		C
ANISOU	1600	CZ	ARG	A	516	1988	1846	2064	22	38	36	A	C		
ATOM	1601	NH1	ARG	A	516	15.789	9.858	29.545	1.00	15.41			A		N
ANISOU	1601	NH1	ARG	A	516	1819	2016	2019	-58	1	-112	A	N		
ATOM	1604	NH2	ARG	A	516	14.335	9.234	31.223	1.00	15.36			A		N
ANISOU	1604	NH2	ARG	A	516	1989	1737	2107	84	31	40	A	N		
ATOM	1607	C	ARG	A	516	20.420	6.252	32.487	1.00	13.71			A		C
ANISOU	1607	C	ARG	A	516	1732	1770	1707	-29	-61	-67	A	C		
ATOM	1608	O	ARG	A	516	21.145	6.580	33.441	1.00	13.82			A		O
ANISOU	1608	O	ARG	A	516	1799	1888	1562	-5	-153	-70	A	O		
ATOM	1609	N	ASN	A	517	19.684	5.140	32.457	1.00	13.59			A		N
ANISOU	1609	N	ASN	A	517	1662	1797	1703	-32	-74	-45	A	N		
ATOM	1611	CA	ASN	A	517	19.450	4.318	33.636	1.00	13.42			A		C
ANISOU	1611	CA	ASN	A	517	1645	1743	1709	-62	-51	-50	A	C		
ATOM	1613	CB	ASN	A	517	17.944	4.137	33.843	1.00	13.51			A		C
ANISOU	1613	CB	ASN	A	517	1669	1766	1697	-8	-46	-16	A	C		
ATOM	1616	CG	ASN	A	517	17.228	5.464	34.078	1.00	13.53			A		C
ANISOU	1616	CG	ASN	A	517	1649	1722	1768	7	-13	-95	A	C		
ATOM	1617	OD1	ASN	A	517	16.266	5.815	33.395	1.00	14.70			A		O
ANISOU	1617	OD1	ASN	A	517	1848	2065	1669	-39	26	-57	A	O		
ATOM	1618	ND2	ASN	A	517	17.701	6.207	35.048	1.00	15.63			A		N

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ANISOU 1618  ND2 ASN A 517     1928   2162   1847     76    -91   -248  A    N
ATOM   1621  C   ASN A 517      20.134   2.969  33.559  1.00 13.65      A    C
ANISOU 1621  C   ASN A 517     1641   1781   1764    -65    -49    -25  A    C
ATOM   1622  O   ASN A 517      19.929   2.120  34.425  1.00 13.34      A    O
ANISOU 1622  O   ASN A 517     1580   1856   1631   -126   -109    -60  A    O
ATOM   1623  N   LYS A 518      20.985   2.790  32.547  1.00 13.68      A    N
ANISOU 1623  N   LYS A 518     1735   1816   1644    -95    -36    -67  A    N
ATOM   1625  CA  LYS A 518      21.658   1.521  32.300  1.00 15.53      A    C
ANISOU 1625  CA  LYS A 518     1950   2007   1942      0     -6     15  A    C
ATOM   1627  CB  LYS A 518      22.707   1.694  31.184  1.00 16.30      A    C
ANISOU 1627  CB  LYS A 518     2067   2115   2008    -32     48      9  A    C
ATOM   1630  CG  LYS A 518      23.666   0.526  31.025  1.00 18.24      A    C
ANISOU 1630  CG  LYS A 518     2292   2325   2311     53    -29     -6  A    C
ATOM   1633  CD  LYS A 518      24.704   0.806  29.928  1.00 21.68      A    C
ANISOU 1633  CD  LYS A 518     2713   2861   2660    -51     70     36  A    C
ATOM   1636  CE  LYS A 518      25.507  -0.446  29.607  1.00 24.34      A    C
ANISOU 1636  CE  LYS A 518     3092   3036   3117      7     11    -38  A    C
ATOM   1639  NZ  LYS A 518      26.330  -0.847  30.773  1.00 26.68      A    N
ANISOU 1639  NZ  LYS A 518     3409   3385   3341      2    -86     44  A    N
ATOM   1643  C   LYS A 518      22.308   0.908  33.526  1.00 15.71      A    C
ANISOU 1643  C   LYS A 518     1935   2014   2017     21     -9      8  A    C
ATOM   1644  O   LYS A 518      22.219  -0.291  33.745  1.00 16.81      A    O
ANISOU 1644  O   LYS A 518     2136   2100   2149     26     -2     34  A    O
ATOM   1645  N   ASN A 519      22.957   1.727  34.327  1.00 15.57      A    N
ANISOU 1645  N   ASN A 519     1971   1985   1957     37     30     11  A    N
ATOM   1647  CA  ASN A 519      23.700   1.193  35.464  1.00 16.90      A    C
ANISOU 1647  CA  ASN A 519     2124   2158   2137      0    -26     17  A    C
ATOM   1649  CB  ASN A 519      24.695   2.234  35.957  1.00 16.82      A    C
ANISOU 1649  CB  ASN A 519     2132   2154   2105     36    -89    -12  A    C
ATOM   1652  CG  ASN A 519      25.788   2.499  34.936  1.00 19.91      A    C
ANISOU 1652  CG  ASN A 519     2455   2632   2477    -38      8      4  A    C
ATOM   1653  OD1 ASN A 519      26.203   1.598  34.193  1.00 24.12      A    O
ANISOU 1653  OD1 ASN A 519     3019   3078   3068     50     74    -56  A    O
ATOM   1654  ND2 ASN A 519      26.259   3.734  34.886  1.00 24.29      A    N
ANISOU 1654  ND2 ASN A 519     3097   2891   3238    -78    155     69  A    N
ATOM   1657  C   ASN A 519      22.830   0.638  36.587  1.00 17.17      A    C
ANISOU 1657  C   ASN A 519     2189   2211   2124     22    -13     23  A    C
ATOM   1658  O   ASN A 519      23.342  -0.091  37.436  1.00 18.51      A    O
ANISOU 1658  O   ASN A 519     2373   2416   2243     16    -31    109  A    O
ATOM   1659  N   SER A 520      21.537   0.961  36.596  1.00 17.98      A    N
ANISOU 1659  N   SER A 520     2283   2363   2183    -37    -51     29  A    N
ATOM   1661  CA  SER A 520      20.621   0.467  37.629  1.00 18.20      A    C
ANISOU 1661  CA  SER A 520     2303   2373   2238    -52      1    -13  A    C
ATOM   1663  CB  SER A 520      19.959   1.652  38.321  1.00 18.86      A    C
ANISOU 1663  CB  SER A 520     2370   2426   2366    -36     50    -19  A    C
ATOM   1666  OG  SER A 520      20.964   2.510  38.840  1.00 20.63      A    O
ANISOU 1666  OG  SER A 520     2612   2716   2511    -84     43    -79  A    O
ATOM   1668  C   SER A 520      19.556  -0.510  37.130  1.00 18.21      A    C
ANISOU 1668  C   SER A 520     2337   2371   2209    -69     34     -4  A    C
ATOM   1669  O   SER A 520      18.767  -1.046  37.904  1.00 19.67      A    O
ANISOU 1669  O   SER A 520     2603   2633   2238   -134    118     16  A    O
ATOM   1670  N   LEU A 521      19.538  -0.766  35.840  1.00 16.22      A    N
ANISOU 1670  N   LEU A 521     2042   2150   1970    -36      7     25  A    N
ATOM   1672  CA  LEU A 521      18.520  -1.634  35.276  1.00 15.83      A    C
ANISOU 1672  CA  LEU A 521     1989   2055   1969    -15     28      9  A    C
ATOM   1674  CB  LEU A 521      18.287  -1.262  33.813  1.00 15.16      A    C
ANISOU 1674  CB  LEU A 521     1924   1969   1865    -43    -38    -18  A    C
ATOM   1677  CG  LEU A 521      17.445  -0.003  33.626  1.00 15.36      A    C
ANISOU 1677  CG  LEU A 521     1994   1996   1846     -3     21     43  A    C
ATOM   1679  CD1 LEU A 521      17.606   0.581  32.220  1.00 14.43      A    C
ANISOU 1679  CD1 LEU A 521     1797   1990   1692    -96    -36    -12  A    C
ATOM   1683  CD2 LEU A 521      16.004  -0.323  33.878  1.00 17.25      A    C
ANISOU 1683  CD2 LEU A 521     2118   2241   2194    -22     19     63  A    C
ATOM   1687  C   LEU A 521      18.896  -3.099  35.387  1.00 15.45      A    C
ANISOU 1687  C   LEU A 521     1923   2011   1935    -10     10     -3  A    C
ATOM   1688  O   LEU A 521      20.030  -3.478  35.084  1.00 17.68      A    O
ANISOU 1688  O   LEU A 521     2097   2275   2345     98    146     45  A    O
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ATOM   1689  N   LYS A 522      17.956  -3.913  35.848  1.00 14.61           A    N
ANISOU 1689  N   LYS A 522    1851   1934   1765     -4      14    -53  A    N
ATOM   1691  CA  LYS A 522      18.112  -5.371  35.897  1.00 14.30           A    C
ANISOU 1691  CA  LYS A 522    1788   1847   1797    -21      -6    -12  A    C
ATOM   1693  CB  LYS A 522      17.216  -5.973  36.987  1.00 14.87           A    C
ANISOU 1693  CB  LYS A 522    1921   1886   1840      1      12     10  A    C
ATOM   1696  CG  LYS A 522      17.466  -5.498  38.395  1.00 17.87           A    C
ANISOU 1696  CG  LYS A 522    2325   2328   2137     57     -25    -72  A    C
ATOM   1699  CD  LYS A 522      16.531  -6.214  39.377  1.00 21.73           A    C
ANISOU 1699  CD  LYS A 522    2777   2767   2710    -86      49     50  A    C
ATOM   1702  CE  LYS A 522      15.213  -5.479  39.565  1.00 24.11           A    C
ANISOU 1702  CE  LYS A 522    3008   3065   3088     26       7      5  A    C
ATOM   1705  NZ  LYS A 522      14.798  -5.470  41.004  1.00 26.70           A    N
ANISOU 1705  NZ  LYS A 522    3500   3390   3253    -35      49      9  A    N
ATOM   1709  C   LYS A 522      17.675  -6.006  34.568  1.00 13.14           A    C
ANISOU 1709  C   LYS A 522    1638   1692   1662    -19      11     17  A    C
ATOM   1710  O   LYS A 522      16.778  -5.503  33.902  1.00 12.43           A    O
ANISOU 1710  O   LYS A 522    1632   1546   1543   -120      15     54  A    O
ATOM   1711  N   VAL A 523      18.255  -7.155  34.230  1.00 12.02           A    N
ANISOU 1711  N   VAL A 523    1542   1542   1479    -43      -2     -9  A    N
ATOM   1713  CA  VAL A 523      17.857  -7.882  33.025  1.00 12.05           A    C
ANISOU 1713  CA  VAL A 523    1557   1579   1441    -36     -11     33  A    C
ATOM   1715  CB  VAL A 523      18.715  -9.145  32.800  1.00 12.93           A    C
ANISOU 1715  CB  VAL A 523    1625   1676   1609     -8      16     -1  A    C
ATOM   1717  CG1 VAL A 523      18.210  -9.948  31.626  1.00 13.27           A    C
ANISOU 1717  CG1 VAL A 523    1660   1675   1706    -11      67     17  A    C
ATOM   1721  CG2 VAL A 523      20.188  -8.786  32.588  1.00 14.25           A    C
ANISOU 1721  CG2 VAL A 523    1800   1944   1669    -68      48     12  A    C
ATOM   1725  C   VAL A 523      16.373  -8.272  33.117  1.00 11.75           A    C
ANISOU 1725  C   VAL A 523    1499   1561   1404    -28     -32     33  A    C
ATOM   1726  O   VAL A 523      15.664  -8.247  32.143  1.00 10.50           A    O
ANISOU 1726  O   VAL A 523    1362   1386   1239    -81    -108    202  A    O
ATOM   1727  N   LEU A 524      15.911  -8.624  34.306  1.00 12.33           A    N
ANISOU 1727  N   LEU A 524    1565   1612   1509    -56     -42     93  A    N
ATOM   1729  CA  LEU A 524      14.514  -8.914  34.560  1.00 13.41           A    C
ANISOU 1729  CA  LEU A 524    1652   1798   1645     -2     -14     69  A    C
ATOM   1731  CB  LEU A 524      14.344  -8.986  36.094  1.00 15.16           A    C
ANISOU 1731  CB  LEU A 524    1890   2012   1855     47     -50    179  A    C
ATOM   1734  CG  LEU A 524      13.061  -9.363  36.763  1.00 20.08           A    C
ANISOU 1734  CG  LEU A 524    2450   2684   2495    -80      45     48  A    C
ATOM   1736  CD1 LEU A 524      12.446 -10.522  36.037  1.00 21.92           A    C
ANISOU 1736  CD1 LEU A 524    2859   2718   2749    -31     -32    -41  A    C
ATOM   1740  CD2 LEU A 524      13.434  -9.741  38.204  1.00 21.61           A    C
ANISOU 1740  CD2 LEU A 524    2929   2684   2597    -69       0     58  A    C
ATOM   1744  C   LEU A 524      13.587  -7.840  33.995  1.00 12.32           A    C
ANISOU 1744  C   LEU A 524    1513   1658   1510    -52     -37     49  A    C
ATOM   1745  O   LEU A 524      12.552  -8.131  33.384  1.00 11.88           A    O
ANISOU 1745  O   LEU A 524    1415   1637   1463   -181     -42    103  A    O
ATOM   1746  N   THR A 525      13.959  -6.590  34.218  1.00 11.05           A    N
ANISOU 1746  N   THR A 525    1336   1613   1247    -93     -20     59  A    N
ATOM   1748  CA  THR A 525      13.190  -5.447  33.789  1.00 10.85           A    C
ANISOU 1748  CA  THR A 525    1328   1497  1296    -65      77      0  A    C
ATOM   1750  CB  THR A 525      13.745  -4.215  34.469  1.00 11.61           A    C
ANISOU 1750  CB  THR A 525    1393   1707   1312    -99      41    -17  A    C
ATOM   1752  OG1 THR A 525      13.715  -4.414  35.900  1.00 12.91           A    O
ANISOU 1752  OG1 THR A 525    1548   2104   1250    -74      20   -137  A    O
ATOM   1754  CG2 THR A 525      12.913  -2.990  34.189  1.00 12.19           A    C
ANISOU 1754  CG2 THR A 525    1507   1718   1407    -66      33   -104  A    C
ATOM   1758  C   THR A 525      13.205  -5.257  32.273  1.00 10.45           A    C
ANISOU 1758  C   THR A 525    1242   1438   1289    -72       6     23  A    C
ATOM   1759  O   THR A 525      12.219  -4.870  31.680  1.00 10.57           A    O
ANISOU 1759  O   THR A 525    1167   1388   1460   -115    -24     34  A    O
ATOM   1760  N   LEU A 526      14.334  -5.549  31.657  1.00  9.36           A    N
ANISOU 1760  N   LEU A 526    1174   1259   1122    -35      -7    -12  A    N
ATOM   1762  CA  LEU A 526      14.460  -5.438  30.215  1.00  9.41           A    C
ANISOU 1762  CA  LEU A 526    1225   1222   1128    -39      -2     43  A    C
ATOM   1764  CB  LEU A 526      15.918  -5.623  29.831  1.00  9.14           A    C
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ANISOU 1764  CB  LEU A 526     1189   1238   1044    -58     36     17  A    C
ATOM   1767  CG  LEU A 526      16.904  -4.618  30.404  1.00  9.74           A    C
ANISOU 1767  CG  LEU A 526     1262   1281   1155     10    -89    -20  A    C
ATOM   1769  CD1 LEU A 526      18.322  -4.916  29.952  1.00 10.71           A    C
ANISOU 1769  CD1 LEU A 526     1380   1362   1325   -103     18    -71  A    C
ATOM   1773  CD2 LEU A 526      16.492  -3.182  30.095  1.00 10.98           A    C
ANISOU 1773  CD2 LEU A 526     1543   1304   1324   -108    -23    -22  A    C
ATOM   1777  C   LEU A 526      13.582  -6.491  29.536  1.00  9.09           A    C
ANISOU 1777  C   LEU A 526     1242   1185   1026    -16     15     -1  A    C
ATOM   1778  O   LEU A 526      12.988  -6.233  28.493  1.00  8.30           A    O
ANISOU 1778  O   LEU A 526     1217    878   1055     41     20     90  A    O
ATOM   1779  N   VAL A 527      13.504  -7.676  30.145  1.00  8.84           A    N
ANISOU 1779  N   VAL A 527     1247   1178    932    -52    -38    -14  A    N
ATOM   1781  CA  VAL A 527      12.645  -8.743  29.661  1.00  9.54           A    C
ANISOU 1781  CA  VAL A 527     1243   1166   1215    -61     12     34  A    C
ATOM   1783  CB  VAL A 527      12.969 -10.092  30.305  1.00  9.86           A    C
ANISOU 1783  CB  VAL A 527     1269   1253   1224     13    -16     10  A    C
ATOM   1785  CG1 VAL A 527      11.984 -11.135  29.857  1.00 11.97           A    C
ANISOU 1785  CG1 VAL A 527     1439   1479   1628    -88      7    109  A    C
ATOM   1789  CG2 VAL A 527      14.369 -10.514  29.931  1.00  9.87           A    C
ANISOU 1789  CG2 VAL A 527     1239   1058   1451    -49      2    -76  A    C
ATOM   1793  C   VAL A 527      11.175  -8.343  29.859  1.00  9.36           A    C
ANISOU 1793  C   VAL A 527     1209   1152   1193    -27    -10    -29  A    C
ATOM   1794  O   VAL A 527      10.343  -8.566  28.983  1.00  9.72           A    O
ANISOU 1794  O   VAL A 527     1239   1278   1175      0    -62    -37  A    O
ATOM   1795  N   LEU A 528      10.860  -7.725  30.994  1.00 10.29           A    N
ANISOU 1795  N   LEU A 528     1267   1299   1344    -42     29    -48  A    N
ATOM   1797  CA  LEU A 528       9.489  -7.280  31.261  1.00 10.35           A    C
ANISOU 1797  CA  LEU A 528     1306   1331   1293    -41      0     35  A    C
ATOM   1799  CB  LEU A 528       9.389  -6.614  32.632  1.00 10.74           A    C
ANISOU 1799  CB  LEU A 528     1459   1244   1375    -78      0     10  A    C
ATOM   1802  CG  LEU A 528       8.064  -5.937  32.926  1.00 12.29           A    C
ANISOU 1802  CG  LEU A 528     1533   1539   1595    -63    -13     20  A    C
ATOM   1804  CD1 LEU A 528       6.941  -6.975  33.017  1.00 13.69           A    C
ANISOU 1804  CD1 LEU A 528     1574   1770   1857   -117     60     20  A    C
ATOM   1808  CD2 LEU A 528       8.153  -5.126  34.181  1.00 13.38           A    C
ANISOU 1808  CD2 LEU A 528     1639   1734   1709     24     52    -63  A    C
ATOM   1812  C   LEU A 528       9.034  -6.300  30.181  1.00  9.90           A    C
ANISOU 1812  C   LEU A 528     1244   1162   1354    -47    -23     41  A    C
ATOM   1813  O   LEU A 528       7.924  -6.413  29.648  1.00 10.14           A    O
ANISOU 1813  O   LEU A 528     1302   1282   1268    -70    -81      0  A    O
ATOM   1814  N   TYR A 529       9.889  -5.317  29.864  1.00  9.63           A    N
ANISOU 1814  N   TYR A 529     1073   1283   1301   -114    -29     47  A    N
ATOM   1816  CA  TYR A 529       9.529  -4.351  28.843  1.00  9.14           A    C
ANISOU 1816  CA  TYR A 529     1094   1143   1236    -17     -8    -11  A    C
ATOM   1818  CB  TYR A 529      10.588  -3.258  28.672  1.00  9.37           A    C
ANISOU 1818  CB  TYR A 529     1153   1152   1252    -53    -18     28  A    C
ATOM   1821  CG  TYR A 529      10.825  -2.388  29.893  1.00 10.76           A    C
ANISOU 1821  CG  TYR A 529     1408   1370   1309     -3     33    -15  A    C
ATOM   1822  CD1 TYR A 529       9.882  -2.244  30.912  1.00 11.31           A    C
ANISOU 1822  CD1 TYR A 529     1491   1376   1427   -184      2   -128  A    C
ATOM   1824  CE1 TYR A 529      10.146  -1.438  32.006  1.00 11.43           A    C
ANISOU 1824  CE1 TYR A 529     1582   1461   1297    -78     31   -171  A    C
ATOM   1826  CZ  TYR A 529      11.352  -0.759  32.072  1.00 12.02           A    C
ANISOU 1826  CZ  TYR A 529     1606   1411   1550    -45    101   -145  A    C
ATOM   1827  OH  TYR A 529      11.660   0.055  33.154  1.00 14.10           A    O
ANISOU 1827  OH  TYR A 529     1938   1820   1597     -4     68   -324  A    O
ATOM   1829  CE2 TYR A 529      12.282  -0.880  31.084  1.00 12.26           A    C
ANISOU 1829  CE2 TYR A 529     1666   1490   1502   -114     47     16  A    C
ATOM   1831  CD2 TYR A 529      12.018  -1.676  30.006  1.00 12.33           A    C
ANISOU 1831  CD2 TYR A 529     1595   1567   1523   -118     67    -77  A    C
ATOM   1833  C   TYR A 529       9.269  -5.030  27.508  1.00  8.97           A    C
ANISOU 1833  C   TYR A 529     1106   1094   1206    -32    -18    -16  A    C
ATOM   1834  O   TYR A 529       8.302  -4.695  26.809  1.00  9.43           A    O
ANISOU 1834  O   TYR A 529     1072   1210   1300    -40     41    -33  A    O
ATOM   1835  N   SER A 530      10.114  -5.992  27.154  1.00  8.94           A    N
ANISOU 1835  N   SER A 530     1036   1132   1229    -61    -24     -9  A    N
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ATOM   1837  CA  SER A 530       9.947  -6.739  25.904  1.00  8.84           A    C
ANISOU 1837  CA  SER A 530    1083   1116   1159    -30     29     37  A    C
ATOM   1839  CB  SER A 530      11.079  -7.742  25.714  1.00  9.23           A    C
ANISOU 1839  CB  SER A 530    1075   1115   1316    -53     14     14  A    C
ATOM   1842  OG  SER A 530      12.340  -7.132  25.627  1.00 10.06           A    O
ANISOU 1842  OG  SER A 530    1121   1154   1545    -63     30    189  A    O
ATOM   1844  C   SER A 530       8.612  -7.473  25.888  1.00  8.46           A    C
ANISOU 1844  C   SER A 530    1026   1096   1092     17     16      2  A    C
ATOM   1845  O   SER A 530       7.913  -7.487  24.889  1.00  8.24           A    O
ANISOU 1845  O   SER A 530     963   1078   1089    132      6     83  A    O
ATOM   1846  N   LEU A 531       8.269  -8.109  27.000  1.00  9.01           A    N
ANISOU 1846  N   LEU A 531    1117   1139   1165    -15    -47     74  A    N
ATOM   1848  CA  LEU A 531       7.001  -8.827  27.133  1.00  8.68           A    C
ANISOU 1848  CA  LEU A 531    1116   1055   1124    -34     27    -56  A    C
ATOM   1850  CB  LEU A 531       6.971  -9.559  28.464  1.00  9.19           A    C
ANISOU 1850  CB  LEU A 531    1163   1088   1240    -14    -28    -50  A    C
ATOM   1853  CG  LEU A 531       5.685 -10.272  28.860  1.00  8.73           A    C
ANISOU 1853  CG  LEU A 531    1172   1052   1091     43     39    -44  A    C
ATOM   1855  CD1 LEU A 531       5.290 -11.366  27.860  1.00  9.70           A    C
ANISOU 1855  CD1 LEU A 531    1345   1059   1281    -62     17    -25  A    C
ATOM   1859  CD2 LEU A 531       5.954 -10.879  30.255  1.00 10.76           A    C
ANISOU 1859  CD2 LEU A 531    1301   1546   1241   -162    132    118  A    C
ATOM   1863  C   LEU A 531       5.796  -7.900  27.005  1.00  9.13           A    C
ANISOU 1863  C   LEU A 531    1146   1127   1193    -21    -18    -57  A    C
ATOM   1864  O   LEU A 531       4.810  -8.224  26.348  1.00  8.80           A    O
ANISOU 1864  O   LEU A 531    1021   1070   1251    -55      1     -6  A    O
ATOM   1865  N   GLN A 532       5.867  -6.732  27.636  1.00  9.21           A    N
ANISOU 1865  N   GLN A 532    1136   1083   1278    -66    -44    -34  A    N
ATOM   1867  CA  GLN A 532       4.768  -5.769  27.593  1.00  9.35           A    C
ANISOU 1867  CA  GLN A 532    1181   1148   1223    -29    -33    -46  A    C
ATOM   1869  CB  GLN A 532       5.110  -4.583  28.474  1.00  9.02           A    C
ANISOU 1869  CB  GLN A 532    1057   1113   1255     99     21   -149  A    C
ATOM   1872  CG  GLN A 532       5.060  -4.948  29.954  1.00  9.32           A    C
ANISOU 1872  CG  GLN A 532    1099   1136   1305      6    -15    -33  A    C
ATOM   1875  CD  GLN A 532       5.341  -3.774  30.882  1.00  9.94           A    C
ANISOU 1875  CD  GLN A 532    1192   1298   1287    -43    -49     15  A    C
ATOM   1876  OE1 GLN A 532       5.859  -2.743  30.446  1.00 10.56           A    O
ANISOU 1876  OE1 GLN A 532    1584   1343   1084   -169    155    -60  A    O
ATOM   1877  NE2 GLN A 532       4.988  -3.930  32.163  1.00 10.28           A    N
ANISOU 1877  NE2 GLN A 532    1277   1497   1130    136    -26   -131  A    N
ATOM   1880  C   GLN A 532       4.512  -5.319  26.166  1.00  8.73           A    C
ANISOU 1880  C   GLN A 532    1089   1053   1175    -12      0    -32  A    C
ATOM   1881  O   GLN A 532       3.382  -5.302  25.727  1.00  9.39           A    O
ANISOU 1881  O   GLN A 532    1118   1217   1231     35    -32    -81  A    O
ATOM   1882  N   ILE A 533       5.572  -4.985  25.435  1.00  8.53           A    N
ANISOU 1882  N   ILE A 533    1058   1056   1127     -3    -11    -22  A    N
ATOM   1884  CA  ILE A 533       5.432  -4.587  24.031  1.00  8.51           A    C
ANISOU 1884  CA  ILE A 533    1073   1079   1081      6     43    -22  A    C
ATOM   1886  CB  ILE A 533       6.751  -4.017  23.491  1.00  9.50           A    C
ANISOU 1886  CB  ILE A 533    1187   1129   1292    -25     -7     -5  A    C
ATOM   1888  CG1 ILE A 533       7.157  -2.772  24.301  1.00  9.86           A    C
ANISOU 1888  CG1 ILE A 533    1199   1147   1398    -86     20    -48  A    C
ATOM   1891  CD1 ILE A 533       6.245  -1.619  24.164  1.00 12.76           A    C
ANISOU 1891  CD1 ILE A 533    1616   1463   1769    -39    -67     67  A    C
ATOM   1895  CG2 ILE A 533       6.651  -3.765  21.994  1.00 10.62           A    C
ANISOU 1895  CG2 ILE A 533    1420   1256   1357    -75    -79     23  A    C
ATOM   1899  C   ILE A 533       4.908  -5.761  23.197  1.00  8.60           A    C
ANISOU 1899  C   ILE A 533    1125   1061   1079    -43    -15     70  A    C
ATOM   1900  O   ILE A 533       4.069  -5.563  22.307  1.00  8.84           A    O
ANISOU 1900  O   ILE A 533    1134   1016   1208     55   -227     -5  A    O
ATOM   1901  N   CYS A 534       5.366  -6.971  23.481  1.00  8.34           A    N
ANISOU 1901  N   CYS A 534    1104   1116    946      6    -90    -22  A    N
ATOM   1903  CA  CYS A 534       4.882  -8.152  22.777  1.00  8.69           A    C
ANISOU 1903  CA  CYS A 534    1093   1101   1105     25    -27    -26  A    C
ATOM   1905  CB  CYS A 534       5.637  -9.377  23.259  1.00  8.61           A    C
ANISOU 1905  CB  CYS A 534    1186    972   1113    -64      7     42  A    C
ATOM   1908  SG  CYS A 534       5.538 -10.759  22.092  1.00  9.98           A    S
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ANISOU 1908  SG  CYS A 534     1431   1011   1350     32   -138   -122  A    S
ATOM   1909  C   CYS A 534       3.375  -8.345  22.957  1.00  8.38        A    C
ANISOU 1909  C   CYS A 534     1059   1083   1039    -15    -58     -4  A    C
ATOM   1910  O   CYS A 534       2.684  -8.727  22.023  1.00  8.76        A    O
ANISOU 1910  O   CYS A 534     1180   1296    851    -32    -39   -122  A    O
ATOM   1911  N   LYS A 535       2.862  -8.093  24.163  1.00  9.20        A    N
ANISOU 1911  N   LYS A 535     1085   1264   1144    -23    -30    -78  A    N
ATOM   1913  CA  LYS A 535       1.428  -8.203  24.428  1.00  9.52        A    C
ANISOU 1913  CA  LYS A 535     1118   1292   1205     32      1    -52  A    C
ATOM   1915  CB  LYS A 535       1.142  -8.059  25.924  1.00  9.70        A    C
ANISOU 1915  CB  LYS A 535     1074   1340   1270    -39     21    -38  A    C
ATOM   1918  CG  LYS A 535       1.581  -9.276  26.716  1.00 12.27        A    C
ANISOU 1918  CG  LYS A 535     1420   1659   1582     44      2     85  A    C
ATOM   1921  CD  LYS A 535       1.302  -9.083  28.189  1.00 15.41        A    C
ANISOU 1921  CD  LYS A 535     1860   2145   1849      6     22    -50  A    C
ATOM   1924  CE  LYS A 535       1.591 -10.341  28.971  1.00 17.41        A    C
ANISOU 1924  CE  LYS A 535     2173   2286   2154    -18     48     28  A    C
ATOM   1927  NZ  LYS A 535       1.182 -10.136  30.386  1.00 20.70        A    N
ANISOU 1927  NZ  LYS A 535     2737   2901   2225     -8    166     51  A    N
ATOM   1931  C   LYS A 535       0.640  -7.181  23.606  1.00  8.70        A    C
ANISOU 1931  C   LYS A 535     1049   1181   1076    -24     37      1  A    C
ATOM   1932  O   LYS A 535      -0.421  -7.489  23.046  1.00  9.75        A    O
ANISOU 1932  O   LYS A 535     1211   1261   1232      4    -35   -141  A    O
ATOM   1933  N   ALA A 536       1.147  -5.957  23.504  1.00  9.18        A    N
ANISOU 1933  N   ALA A 536     1196   1172   1118     61    -42    -76  A    N
ATOM   1935  CA  ALA A 536       0.544  -4.974  22.601  1.00  8.93        A    C
ANISOU 1935  CA  ALA A 536     1079   1204   1110    100     23    -34  A    C
ATOM   1937  CB  ALA A 536       1.287  -3.675  22.658  1.00  9.97        A    C
ANISOU 1937  CB  ALA A 536     1288   1240   1258    112     22    -85  A    C
ATOM   1941  C   ALA A 536       0.475  -5.497  21.174  1.00  8.90        A    C
ANISOU 1941  C   ALA A 536     1051   1234   1093     62    -53    -63  A    C
ATOM   1942  O   ALA A 536      -0.541  -5.348  20.486  1.00  9.18        A    O
ANISOU 1942  O   ALA A 536      977   1349   1159    187      9     36  A    O
ATOM   1943  N   MET A 537       1.576  -6.078  20.703  1.00  8.38        A    N
ANISOU 1943  N   MET A 537      969   1184   1029     69    -70    -27  A    N
ATOM   1945  CA  MET A 537       1.656  -6.598  19.345  1.00  9.14        A    C
ANISOU 1945  CA  MET A 537     1075   1257   1137     52    -34    -32  A    C
ATOM   1947  CB  MET A 537       3.106  -6.895  18.960  1.00  9.20        A    C
ANISOU 1947  CB  MET A 537     1148   1184   1161    137     12   -128  A    C
ATOM   1950  CG  MET A 537       3.944  -5.630  18.797  1.00 11.09        A    C
ANISOU 1950  CG  MET A 537     1223   1582   1409    -13     94   -197  A    C
ATOM   1953  SD  MET A 537       3.206  -4.382  17.684  1.00 13.43        A    S
ANISOU 1953  SD  MET A 537     1844   1254   2003     62    403    -32  A    S
ATOM   1954  CE  MET A 537       2.792  -5.416  16.235  1.00 14.20        A    C
ANISOU 1954  CE  MET A 537     1922   1653   1819    134    102    123  A    C
ATOM   1958  C   MET A 537       0.755  -7.791  19.132  1.00  8.69        A    C
ANISOU 1958  C   MET A 537     1067   1175   1057     69      4    -23  A    C
ATOM   1959  O   MET A 537       0.191  -7.938  18.045  1.00  9.24        A    O
ANISOU 1959  O   MET A 537      975   1485   1050    118    -55     -9  A    O
ATOM   1960  N   ALA A 538       0.561  -8.635  20.147  1.00  9.38        A    N
ANISOU 1960  N   ALA A 538     1213   1268   1083    -14    -77      2  A    N
ATOM   1962  CA  ALA A 538      -0.374  -9.741  20.011  1.00  8.94        A    C
ANISOU 1962  CA  ALA A 538     1177   1182   1038      5    -33    -35  A    C
ATOM   1964  CB  ALA A 538      -0.346 -10.626  21.231  1.00  9.08        A    C
ANISOU 1964  CB  ALA A 538     1141   1074   1233     14     11     53  A    C
ATOM   1968  C   ALA A 538      -1.774  -9.180  19.782  1.00  9.51        A    C
ANISOU 1968  C   ALA A 538     1216   1276   1121    -11     -1    -55  A    C
ATOM   1969  O   ALA A 538      -2.557  -9.735  18.995  1.00  9.57        A    O
ANISOU 1969  O   ALA A 538     1046   1423   1164    -75    -73   -128  A    O
ATOM   1970  N   TYR A 539      -2.114  -8.092  20.457  1.00  9.75        A    N
ANISOU 1970  N   TYR A 539     1179   1314   1212     21      7    -38  A    N
ATOM   1972  CA  TYR A 539      -3.407  -7.484  20.197  1.00 10.52        A    C
ANISOU 1972  CA  TYR A 539     1245   1384   1367     53     17    -64  A    C
ATOM   1974  CB  TYR A 539      -3.710  -6.383  21.215  1.00 11.10        A    C
ANISOU 1974  CB  TYR A 539     1436   1402   1380    -26      9    -83  A    C
ATOM   1977  CG  TYR A 539      -4.991  -5.665  20.906  1.00 12.72        A    C
ANISOU 1977  CG  TYR A 539     1627   1769   1436    156     88   -137  A    C
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ATOM   1978  CD1 TYR A 539      -6.187  -6.360  20.802  1.00 15.35           A    C
ANISOU 1978  CD1 TYR A 539     1903   1979   1949     56     81    -13  A    C
ATOM   1980  CE1 TYR A 539      -7.383  -5.734  20.478  1.00 17.27           A    C
ANISOU 1980  CE1 TYR A 539     2084   2223   2252     46     85     78  A    C
ATOM   1982  CZ  TYR A 539      -7.407  -4.392  20.279  1.00 17.42           A    C
ANISOU 1982  CZ  TYR A 539     2158   2210   2248    154    128    -16  A    C
ATOM   1983  OH  TYR A 539      -8.635  -3.817  19.972  1.00 20.79           A    O
ANISOU 1983  OH  TYR A 539     2483   2758   2656    265   -154    102  A    O
ATOM   1985  CE2 TYR A 539      -6.236  -3.650  20.387  1.00 18.14           A    C
ANISOU 1985  CE2 TYR A 539     2265   2231   2395    131    -31     -7  A    C
ATOM   1987  CD2 TYR A 539      -5.011  -4.305  20.687  1.00 16.60           A    C
ANISOU 1987  CD2 TYR A 539     2066   2069   2170     14    174     55  A    C
ATOM   1989  C   TYR A 539      -3.509  -6.967  18.769  1.00  9.93           A    C
ANISOU 1989  C   TYR A 539     1089   1354   1330    -21      5    -61  A    C
ATOM   1990  O   TYR A 539      -4.509  -7.190  18.067  1.00 10.52           A    O
ANISOU 1990  O   TYR A 539      989   1647   1358     17     32    -85  A    O
ATOM   1991  N   LEU A 540      -2.499  -6.223  18.310  1.00  9.16           A    N
ANISOU 1991  N   LEU A 540      994   1270   1216     24     13     23  A    N
ATOM   1993  CA  LEU A 540      -2.551  -5.753  16.947  1.00  9.93           A    C
ANISOU 1993  CA  LEU A 540     1148   1347   1277     11    -27      8  A    C
ATOM   1995  CB  LEU A 540      -1.383  -4.793  16.676  1.00 10.30           A    C
ANISOU 1995  CB  LEU A 540     1226   1342   1344    -27     43     27  A    C
ATOM   1998  CG  LEU A 540      -1.357  -3.503  17.527  1.00 11.55           A    C
ANISOU 1998  CG  LEU A 540     1448   1487   1453     24     27     10  A    C
ATOM   2000  CD1 LEU A 540      -0.182  -2.587  17.170  1.00 13.03           A    C
ANISOU 2000  CD1 LEU A 540     1510   1623   1818     12     59    -30  A    C
ATOM   2004  CD2 LEU A 540      -2.683  -2.769  17.444  1.00 10.93           A    C
ANISOU 2004  CD2 LEU A 540     1550   1247   1357     92     -1     -6  A    C
ATOM   2008  C   LEU A 540      -2.607  -6.914  15.941  1.00  9.95           A    C
ANISOU 2008  C   LEU A 540     1155   1333   1291     37     17      7  A    C
ATOM   2009  O   LEU A 540      -3.339  -6.847  14.957  1.00 10.84           A    O
ANISOU 2009  O   LEU A 540     1157   1574   1385    137   -103    -57  A    O
ATOM   2010  N   GLU A 541      -1.883  -7.994  16.183  1.00 10.20           A    N
ANISOU 2010  N   GLU A 541     1222   1390   1263     21   -127     20  A    N
ATOM   2012  CA  GLU A 541      -1.942  -9.177  15.318  1.00 10.92           A    C
ANISOU 2012  CA  GLU A 541     1338   1411   1397     77     13    -17  A    C
ATOM   2014  CB  GLU A 541      -1.027 -10.256  15.898  1.00 11.79           A    C
ANISOU 2014  CB  GLU A 541     1402   1554   1523     95    -62    -29  A    C
ATOM   2017  CG  GLU A 541      -1.082 -11.616  15.227  1.00 11.44           A    C
ANISOU 2017  CG  GLU A 541     1248   1518   1580    -19    -74     21  A    C
ATOM   2020  CD  GLU A 541      -0.083 -12.570  15.866  1.00 12.04           A    C
ANISOU 2020  CD  GLU A 541     1463   1421   1690    -44   -118     32  A    C
ATOM   2021  OE1 GLU A 541      -0.394 -13.132  16.937  1.00 13.20           A    O
ANISOU 2021  OE1 GLU A 541     1418   1892   1704     30   -170    155  A    O
ATOM   2022  OE2 GLU A 541       1.026 -12.690  15.331  1.00 12.85           A    O
ANISOU 2022  OE2 GLU A 541     1700   1601   1579     52    -98     24  A    O
ATOM   2023  C   GLU A 541      -3.384  -9.717  15.198  1.00 11.01           A    C
ANISOU 2023  C   GLU A 541     1417   1423   1343     15    -37    -51  A    C
ATOM   2024  O   GLU A 541      -3.814 -10.155  14.129  1.00 11.07           A    O
ANISOU 2024  O   GLU A 541     1329   1472   1405    115    -37   -127  A    O
ATOM   2025  N   SER A 542      -4.131  -9.666  16.305  1.00 11.07           A    N
ANISOU 2025  N   SER A 542     1333   1456   1416     -4     25    -35  A    N
ATOM   2027  CA  SER A 542      -5.476 -10.210  16.354  1.00 11.62           A    C
ANISOU 2027  CA  SER A 542     1396   1549   1468    -28    -12    -29  A    C
ATOM   2029  CB  SER A 542      -6.005 -10.237  17.795  1.00 11.54           A    C
ANISOU 2029  CB  SER A 542     1344   1574   1466    -76     -6    -61  A    C
ATOM   2032  OG  SER A 542      -6.484  -8.971  18.196  1.00 12.72           A    O
ANISOU 2032  OG  SER A 542     1330   1755   1747     50     49     71  A    O
ATOM   2034  C   SER A 542      -6.447  -9.463  15.454  1.00 12.29           A    C
ANISOU 2034  C   SER A 542     1429   1642   1599    -30    -14    -12  A    C
ATOM   2035  O   SER A 542      -7.479 -10.038  15.085  1.00 13.05           A    O
ANISOU 2035  O   SER A 542     1416   1883   1658   -148    -85    -25  A    O
ATOM   2036  N   ILE A 543      -6.139  -8.203  15.125  1.00 12.06           A    N
ANISOU 2036  N   ILE A 543     1377   1609   1595      0    -50     -3  A    N
ATOM   2038  CA  ILE A 543      -6.927  -7.427  14.167  1.00 12.89           A    C
ANISOU 2038  CA  ILE A 543     1507   1753   1636    -22    -12     33  A    C
ATOM   2040  CB  ILE A 543      -7.411  -6.101  14.786  1.00 12.91           A    C
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ANISOU 2040  CB  ILE A 543     1456   1795   1651    -11    -59     38  A    C
ATOM   2042  CG1 ILE A 543      -6.272  -5.280  15.408  1.00 12.95      A    C
ANISOU 2042  CG1 ILE A 543     1623   1687   1610    -26    -51    -33  A    C
ATOM   2045  CD1 ILE A 543      -6.660  -3.826  15.644  1.00 14.46      A    C
ANISOU 2045  CD1 ILE A 543     1779   1755   1957    -27     -7     16  A    C
ATOM   2049  CG2 ILE A 543      -8.465  -6.376  15.826  1.00 13.78      A    C
ANISOU 2049  CG2 ILE A 543     1634   1876   1723     -8     28     56  A    C
ATOM   2053  C   ILE A 543      -6.184  -7.192  12.848  1.00 13.59      A    C
ANISOU 2053  C   ILE A 543     1727   1794   1639     65    -11     29  A    C
ATOM   2054  O   ILE A 543      -6.597  -6.361  12.034  1.00 14.94      A    O
ANISOU 2054  O   ILE A 543     1834   1982   1858    192     28    151  A    O
ATOM   2055  N   ASN A 544      -5.142  -7.979  12.594  1.00 14.05      A    N
ANISOU 2055  N   ASN A 544     1657   1897   1781     79    -75     20  A    N
ATOM   2057  CA  ASN A 544      -4.333  -7.838  11.388  1.00 15.80      A    C
ANISOU 2057  CA  ASN A 544     1991   2045   1965     65    -36     67  A    C
ATOM   2059  CB  ASN A 544      -5.136  -8.340  10.164  1.00 17.02      A    C
ANISOU 2059  CB  ASN A 544     2179   2222   2064     22      4     13  A    C
ATOM   2062  CG  ASN A 544      -5.600  -9.780  10.307  1.00 21.95      A    C
ANISOU 2062  CG  ASN A 544     2855   2660   2822    -52    -23     11  A    C
ATOM   2063  OD1 ASN A 544      -4.820 -10.658  10.687  1.00 26.38      A    O
ANISOU 2063  OD1 ASN A 544     3448   3186   3389    242   -102    106  A    O
ATOM   2064  ND2 ASN A 544      -6.864 -10.045   9.950  1.00 25.54      A    N
ANISOU 2064  ND2 ASN A 544     3002   3389   3311    -28     -9    -30  A    N
ATOM   2067  C   ASN A 544      -3.839  -6.386  11.145  1.00 15.07      A    C
ANISOU 2067  C   ASN A 544     1894   1964   1866     91     -6     -2  A    C
ATOM   2068  O   ASN A 544      -3.784  -5.914   9.982  1.00 16.47      A    O
ANISOU 2068  O   ASN A 544     2180   2149   1928    174      0     10  A    O
ATOM   2069  N   CAS A 545      -3.491  -5.677  12.224  1.00 14.03      A    N
ANISOU 2069  N   CAS A 545     1635   1857   1837     69    -40     25  A    N
ATOM   2072  CA  CAS A 545      -2.959  -4.333  12.145  1.00 14.24      A    C
ANISOU 2072  CA  CAS A 545     1745   1849   1815     34    -17     35  A    C
ATOM   2074  CB  CAS A 545      -3.448  -3.554  13.346  1.00 15.02      A    C
ANISOU 2074  CB  CAS A 545     1838   1878   1988    126     45     43  A    C
ATOM   2077  SG  CAS A 545      -2.801  -1.903  13.461  1.00 19.61      A    S
ANISOU 2077  SG  CAS A 545     2777   2151   2522    186     47    -59  A    S
ATOM   2078 AS   CAS A 545      -3.902  -0.995  11.780  0.50 18.37      A   AS
ANISOU 2078 AS   CAS A 545     2487   1666   2824    158   -103     26  A   AS
ATOM   2079  CE2 CAS A 545      -2.576  -0.647  10.336  0.50 20.07      A    C
ANISOU 2079  CE2 CAS A 545     2571   2431   2622     30    -72     10  A    C
ATOM   2083  CE1 CAS A 545      -5.056   0.534  12.278  0.50 19.01      A    C
ANISOU 2083  CE1 CAS A 545     2429   2292   2501    113     41    -93  A    C
ATOM   2087  C   CAS A 545      -1.460  -4.413  12.155  1.00 13.38      A    C
ANISOU 2087  C   CAS A 545     1637   1815   1631     44     10     77  A    C
ATOM   2088  O   CAS A 545      -0.842  -4.851  13.112  1.00 13.52      A    O
ANISOU 2088  O   CAS A 545     1605   1982   1548     57     61    268  A    O
ATOM   2090  N   VAL A 546      -0.859  -3.933  11.077  1.00 12.64      A    N
ANISOU 2090  N   VAL A 546     1604   1635   1564     30     75     33  A    N
ATOM   2092  CA  VAL A 546       0.573  -3.935  10.899  1.00 12.23      A    C
ANISOU 2092  CA  VAL A 546     1538   1611   1495     23    -29     30  A    C
ATOM   2094  CB  VAL A 546       0.954  -4.245   9.452  1.00 13.05      A    C
ANISOU 2094  CB  VAL A 546     1613   1713   1629     -1     40      8  A    C
ATOM   2096  CG1 VAL A 546       2.485  -4.277   9.302  1.00 13.38      A    C
ANISOU 2096  CG1 VAL A 546     1660   1832   1590    -66     88    116  A    C
ATOM   2100  CG2 VAL A 546       0.343  -5.567   9.029  1.00 13.89      A    C
ANISOU 2100  CG2 VAL A 546     1761   1847   1666     16     36    -13  A    C
ATOM   2104  C   VAL A 546       1.094  -2.574  11.315  1.00 11.11      A    C
ANISOU 2104  C   VAL A 546     1416   1456   1345    100     99     15  A    C
ATOM   2105  O   VAL A 546       0.762  -1.552  10.731  1.00 13.61      A    O
ANISOU 2105  O   VAL A 546     1681   1729   1759    139     13    126  A    O
ATOM   2106  N   HIS A 547       1.967  -2.572  12.311  1.00 10.67      A    N
ANISOU 2106  N   HIS A 547     1441   1290   1322    105     26     21  A    N
ATOM   2108  CA  HIS A 547       2.375  -1.352  12.978  1.00 10.61      A    C
ANISOU 2108  CA  HIS A 547     1372   1346   1311     60    -25    -23  A    C
ATOM   2110  CB  HIS A 547       2.737  -1.689  14.403  1.00 11.17      A    C
ANISOU 2110  CB  HIS A 547     1466   1408   1369     -5     14    -20  A    C
ATOM   2113  CG  HIS A 547       2.988  -0.500  15.257  1.00 10.55      A    C
ANISOU 2113  CG  HIS A 547     1326   1212   1467    214    -53     50  A    C
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ATOM   2114  ND1 HIS A 547      4.222   0.091  15.347  1.00 12.47           A    N
ANISOU 2114  ND1 HIS A 547     1647   1680   1409   -129   -130     10  A    N
ATOM   2116  CE1 HIS A 547      4.168   1.092  16.208  1.00 12.36           A    C
ANISOU 2116  CE1 HIS A 547     1532   1430   1733     96     25    -63  A    C
ATOM   2118  NE2 HIS A 547      2.921   1.215  16.623  1.00 13.17           A    N
ANISOU 2118  NE2 HIS A 547     1459   1693   1850    -47     -9      0  A    N
ATOM   2120  CD2 HIS A 547      2.165   0.228  16.042  1.00 11.72           A    C
ANISOU 2120  CD2 HIS A 547     1379   1402   1672    153     89    -94  A    C
ATOM   2122  C   HIS A 547      3.515  -0.604  12.297  1.00 11.31           A    C
ANISOU 2122  C   HIS A 547     1513   1402   1379     42    -12     -8  A    C
ATOM   2123  O   HIS A 547      3.443   0.608  12.112  1.00 12.83           A    O
ANISOU 2123  O   HIS A 547     1672   1536   1665     78    -21    -30  A    O
ATOM   2124  N   ARG A 548      4.564  -1.342  11.938  1.00 11.57           A    N
ANISOU 2124  N   ARG A 548     1449   1460   1487     61    -12     93  A    N
ATOM   2126  CA  ARG A 548      5.723  -0.839  11.208  1.00 11.95           A    C
ANISOU 2126  CA  ARG A 548     1411   1558   1568     50     24     42  A    C
ATOM   2128  CB  ARG A 548      5.324  -0.106   9.919  1.00 12.37           A    C
ANISOU 2128  CB  ARG A 548     1407   1690   1600     23     42     63  A    C
ATOM   2131  CG  ARG A 548      4.400  -0.860   9.000  1.00 12.27           A    C
ANISOU 2131  CG  ARG A 548     1419   1656   1584     58     73      1  A    C
ATOM   2134  CD  ARG A 548      4.245  -0.126   7.686  1.00 14.56           A    C
ANISOU 2134  CD  ARG A 548     1895   1865   1769     49     23     31  A    C
ATOM   2137  NE  ARG A 548      3.276  -0.702   6.768  1.00 14.69           A    N
ANISOU 2137  NE  ARG A 548     1963   1899   1720     78    -18    120  A    N
ATOM   2139  CZ  ARG A 548      3.282  -0.444   5.464  1.00 15.09           A    C
ANISOU 2139  CZ  ARG A 548     2009   1966   1758    -45     23     -4  A    C
ATOM   2140  NH1 ARG A 548      4.174   0.391   4.974  1.00 14.76           A    N
ANISOU 2140  NH1 ARG A 548     2013   2073   1519    -47     62    -21  A    N
ATOM   2143  NH2 ARG A 548      2.390  -0.992   4.656  1.00 16.02           A    N
ANISOU 2143  NH2 ARG A 548     1971   2124   1989    -61     16     -2  A    N
ATOM   2146  C   ARG A 548      6.693   0.072  11.955  1.00 11.43           A    C
ANISOU 2146  C   ARG A 548     1385   1419   1538     46     35     92  A    C
ATOM   2147  O   ARG A 548      7.658   0.531  11.349  1.00 13.42           A    O
ANISOU 2147  O   ARG A 548     1435   1793   1868     36     56    223  A    O
ATOM   2148  N   ASP A 549      6.448   0.383  13.222  1.00 12.01           A    N
ANISOU 2148  N   ASP A 549     1462   1490   1609     38     34     30  A    N
ATOM   2150  CA  ASP A 549      7.341   1.272  13.975  1.00 12.94           A    C
ANISOU 2150  CA  ASP A 549     1595   1591   1729     97    -48    -30  A    C
ATOM   2152  CB  ASP A 549      6.878   2.731  13.931  1.00 14.09           A    C
ANISOU 2152  CB  ASP A 549     1785   1668   1897    107    -31     -8  A    C
ATOM   2155  CG  ASP A 549      7.986   3.712  14.315  1.00 17.92           A    C
ANISOU 2155  CG  ASP A 549     2227   2112   2468    -45    -18    -21  A    C
ATOM   2156  OD1 ASP A 549      9.171   3.291  14.479  1.00 21.77           A    O
ANISOU 2156  OD1 ASP A 549     2568   2693   3008      6   -101    112  A    O
ATOM   2157  OD2 ASP A 549      7.742   4.937  14.480  1.00 20.33           A    O
ANISOU 2157  OD2 ASP A 549     2780   2082   2862   -148     25    -17  A    O
ATOM   2158  C   ASP A 549      7.551   0.816  15.392  1.00 12.24           A    C
ANISOU 2158  C   ASP A 549     1466   1528   1654     51      0    -32  A    C
ATOM   2159  O   ASP A 549      7.316   1.550  16.367  1.00 13.22           A    O
ANISOU 2159  O   ASP A 549     1691   1621   1707    143   -155   -110  A    O
ATOM   2160  N   ILE A 550      8.025  -0.419  15.499  1.00 11.46           A    N
ANISOU 2160  N   ILE A 550     1425   1417   1512     57    -51    -47  A    N
ATOM   2162  CA  ILE A 550      8.294  -1.047  16.778  1.00 10.66           A    C
ANISOU 2162  CA  ILE A 550     1268   1415   1364     33    -30    -53  A    C
ATOM   2164  CB  ILE A 550      7.904  -2.528  16.745  1.00 10.39           A    C
ANISOU 2164  CB  ILE A 550     1208   1351   1388     60     31    -26  A    C
ATOM   2166  CG1 ILE A 550      6.497  -2.712  16.183  1.00 11.03           A    C
ANISOU 2166  CG1 ILE A 550     1285   1371   1532    -38    -61    -29  A    C
ATOM   2169  CD1 ILE A 550      6.253  -4.071  15.615  1.00 13.07           A    C
ANISOU 2169  CD1 ILE A 550     1555   1625   1784    -13     56   -101  A    C
ATOM   2173  CG2 ILE A 550      7.997  -3.106  18.142  1.00 12.08           A    C
ANISOU 2173  CG2 ILE A 550     1455   1598   1536    164     -6     62  A    C
ATOM   2177  C   ILE A 550      9.791  -0.900  17.051  1.00 10.76           A    C
ANISOU 2177  C   ILE A 550     1253   1424   1410     79    -60    -75  A    C
ATOM   2178  O   ILE A 550     10.636  -1.635  16.527  1.00 11.52           A    O
ANISOU 2178  O   ILE A 550     1347   1415   1612    152   -124   -125  A    O
ATOM   2179  N   ALA A 551     10.109   0.131  17.820  1.00 10.63           A    N
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ANISOU	2179	N	ALA	A	551	1251	1325	1461	83	-64	-113	A	N
ATOM	2181	CA	ALA	A	551	11.484	0.550	18.071	1.00	10.00		A	C
ANISOU	2181	CA	ALA	A	551	1231	1250	1316	-1	-10	4	A	C
ATOM	2183	CB	ALA	A	551	11.996	1.385	16.909	1.00	9.71		A	C
ANISOU	2183	CB	ALA	A	551	1162	1199	1328	31	97	-38	A	C
ATOM	2187	C	ALA	A	551	11.503	1.365	19.339	1.00	9.46		A	C
ANISOU	2187	C	ALA	A	551	1166	1222	1206	-13	39	33	A	C
ATOM	2188	O	ALA	A	551	10.511	1.990	19.683	1.00	11.05		A	O
ANISOU	2188	O	ALA	A	551	1324	1408	1464	6	-41	22	A	O
ATOM	2189	N	VAL	A	552	12.635	1.376	20.041	1.00	9.14		A	N
ANISOU	2189	N	VAL	A	552	1102	1081	1290	47	5	12	A	N
ATOM	2191	CA	VAL	A	552	12.676	2.000	21.365	1.00	9.60		A	C
ANISOU	2191	CA	VAL	A	552	1211	1209	1227	-10	-2	34	A	C
ATOM	2193	CB	VAL	A	552	13.970	1.684	22.161	1.00	9.79		A	C
ANISOU	2193	CB	VAL	A	552	1144	1219	1354	59	24	-80	A	C
ATOM	2195	CG1	VAL	A	552	14.040	0.209	22.482	1.00	10.22		A	C
ANISOU	2195	CG1	VAL	A	552	1205	1269	1408	7	50	124	A	C
ATOM	2199	CG2	VAL	A	552	15.209	2.196	21.483	1.00	9.58		A	C
ANISOU	2199	CG2	VAL	A	552	1119	1259	1260	-6	-30	-85	A	C
ATOM	2203	C	VAL	A	552	12.450	3.506	21.350	1.00	10.58		A	C
ANISOU	2203	C	VAL	A	552	1321	1273	1426	-3	55	-57	A	C
ATOM	2204	O	VAL	A	552	11.957	4.074	22.343	1.00	11.27		A	O
ANISOU	2204	O	VAL	A	552	1553	1429	1301	-2	-9	-61	A	O
ATOM	2205	N	ARG	A	553	12.780	4.150	20.234	1.00	11.21		A	N
ANISOU	2205	N	ARG	A	553	1477	1382	1400	14	22	-86	A	N
ATOM	2207	CA	ARG	A	553	12.497	5.572	20.061	1.00	12.16		A	C
ANISOU	2207	CA	ARG	A	553	1563	1432	1624	27	22	-24	A	C
ATOM	2209	CB	ARG	A	553	13.143	6.078	18.762	1.00	13.88		A	C
ANISOU	2209	CB	ARG	A	553	1762	1701	1810	-26	73	47	A	C
ATOM	2212	CG	ARG	A	553	12.998	7.551	18.453	1.00	18.30		A	C
ANISOU	2212	CG	ARG	A	553	2397	2089	2467	108	26	-58	A	C
ATOM	2215	CD	ARG	A	553	13.731	7.938	17.160	1.00	23.71		A	C
ANISOU	2215	CD	ARG	A	553	3003	3086	2919	2	123	87	A	C
ATOM	2218	NE	ARG	A	553	13.755	9.366	16.854	1.00	28.74		A	N
ANISOU	2218	NE	ARG	A	553	3758	3444	3716	39	11	10	A	N
ATOM	2220	CZ	ARG	A	553	14.289	9.867	15.739	1.00	31.75		A	C
ANISOU	2220	CZ	ARG	A	553	4090	4001	3971	-14	71	59	A	C
ATOM	2221	NH1	ARG	A	553	14.846	9.063	14.832	1.00	33.43		A	N
ANISOU	2221	NH1	ARG	A	553	4320	4210	4169	56	86	-3	A	N
ATOM	2224	NH2	ARG	A	553	14.265	11.172	15.519	1.00	32.88		A	N
ANISOU	2224	NH2	ARG	A	553	4281	4027	4185	-14	48	26	A	N
ATOM	2227	C	ARG	A	553	10.973	5.833	20.053	1.00	11.70		A	C
ANISOU	2227	C	ARG	A	553	1522	1383	1538	48	10	-29	A	C
ATOM	2228	O	ARG	A	553	10.533	6.955	20.301	1.00	13.49		A	O
ANISOU	2228	O	ARG	A	553	1766	1425	1932	29	37	-158	A	O
ATOM	2229	N	ASN	A	554	10.197	4.801	19.754	1.00	11.17		A	N
ANISOU	2229	N	ASN	A	554	1357	1334	1550	21	65	-9	A	N
ATOM	2231	CA	ASN	A	554	8.738	4.884	19.635	1.00	10.72		A	C
ANISOU	2231	CA	ASN	A	554	1330	1319	1424	-13	17	-55	A	C
ATOM	2233	CB	ASN	A	554	8.249	4.432	18.249	1.00	10.62		A	C
ANISOU	2233	CB	ASN	A	554	1364	1352	1318	-1	24	6	A	C
ATOM	2236	CG	ASN	A	554	6.807	4.871	17.959	1.00	12.01		A	C
ANISOU	2236	CG	ASN	A	554	1478	1588	1496	29	19	-117	A	C
ATOM	2237	OD1	ASN	A	554	6.403	5.973	18.358	1.00	15.71		A	O
ANISOU	2237	OD1	ASN	A	554	1886	1664	2416	172	72	-49	A	O
ATOM	2238	ND2	ASN	A	554	6.032	4.018	17.285	1.00	12.82		A	N
ANISOU	2238	ND2	ASN	A	554	1674	1585	1609	-3	135	-79	A	N
ATOM	2241	C	ASN	A	554	8.007	4.096	20.708	1.00	10.60		A	C
ANISOU	2241	C	ASN	A	554	1285	1399	1341	-2	59	-65	A	C
ATOM	2242	O	ASN	A	554	6.889	3.651	20.506	1.00	11.82		A	O
ANISOU	2242	O	ASN	A	554	1334	1668	1489	-37	93	-58	A	O
ATOM	2243	N	ILE	A	555	8.660	3.897	21.840	1.00	10.92		A	N
ANISOU	2243	N	ILE	A	555	1279	1524	1344	-102	94	22	A	N
ATOM	2245	CA	ILE	A	555	8.053	3.329	23.036	1.00	10.52		A	C
ANISOU	2245	CA	ILE	A	555	1291	1427	1278	-43	91	-30	A	C
ATOM	2247	CB	ILE	A	555	8.726	2.024	23.412	1.00	10.98		A	C
ANISOU	2247	CB	ILE	A	555	1399	1514	1258	-86	80	5	A	C

ATOM	2249	CG1	ILE	A	555	8.482	0.986	22.302	1.00	12.83			A	C
ANISOU	2249	CG1	ILE	A	555	1727	1630	1516	-14	167	-14		A	C
ATOM	2252	CD1	ILE	A	555	9.354	-0.148	22.390	1.00	13.57			A	C
ANISOU	2252	CD1	ILE	A	555	1552	1857	1745	0	106	-62		A	C
ATOM	2256	CG2	ILE	A	555	8.210	1.549	24.788	1.00	11.79			A	C
ANISOU	2256	CG2	ILE	A	555	1433	1656	1389	-19	194	59		A	C
ATOM	2260	C	ILE	A	555	8.206	4.369	24.127	1.00	10.30			A	C
ANISOU	2260	C	ILE	A	555	1241	1376	1295	-57	13	-9		A	C
ATOM	2261	O	ILE	A	555	9.261	4.978	24.271	1.00	10.45			A	O
ANISOU	2261	O	ILE	A	555	1336	1295	1337	-131	107	-9		A	O
ATOM	2262	N	LEU	A	556	7.125	4.598	24.858	1.00	10.78			A	N
ANISOU	2262	N	LEU	A	556	1288	1442	1364	-37	39	-96		A	N
ATOM	2264	CA	LEU	A	556	7.109	5.589	25.924	1.00	11.49			A	C
ANISOU	2264	CA	LEU	A	556	1447	1438	1479	-15	37	-69		A	C
ATOM	2266	CB	LEU	A	556	5.922	6.560	25.755	1.00	12.91			A	C
ANISOU	2266	CB	LEU	A	556	1553	1603	1748	76	34	-120		A	C
ATOM	2269	CG	LEU	A	556	5.973	7.473	24.521	1.00	16.23			A	C
ANISOU	2269	CG	LEU	A	556	1988	2084	2094	48	54	26		A	C
ATOM	2271	CD1	LEU	A	556	4.806	8.420	24.478	1.00	20.11			A	C
ANISOU	2271	CD1	LEU	A	556	2429	2590	2621	132	-85	24		A	C
ATOM	2275	CD2	LEU	A	556	7.232	8.281	24.391	1.00	18.33			A	C
ANISOU	2275	CD2	LEU	A	556	2313	2157	2494	-49	-71	37		A	C
ATOM	2279	C	LEU	A	556	7.099	4.924	27.264	1.00	11.18			A	C
ANISOU	2279	C	LEU	A	556	1411	1350	1486	-8	5	-68		A	C
ATOM	2280	O	LEU	A	556	6.497	3.875	27.443	1.00	10.88			A	O
ANISOU	2280	O	LEU	A	556	1435	1321	1375	-47	107	-217		A	O
ATOM	2281	N	VAL	A	557	7.798	5.531	28.216	1.00	10.68			A	N
ANISOU	2281	N	VAL	A	557	1407	1295	1354	-64	15	-94		A	N
ATOM	2283	CA	VAL	A	557	7.917	4.967	29.558	1.00	10.69			A	C
ANISOU	2283	CA	VAL	A	557	1364	1324	1373	10	-2	-46		A	C
ATOM	2285	CB	VAL	A	557	9.334	5.102	30.117	1.00	10.98			A	C
ANISOU	2285	CB	VAL	A	557	1382	1355	1434	-61	39	-51		A	C
ATOM	2287	CG1	VAL	A	557	9.415	4.495	31.502	1.00	10.58			A	C
ANISOU	2287	CG1	VAL	A	557	1261	1241	1516	73	32	-44		A	C
ATOM	2291	CG2	VAL	A	557	10.350	4.474	29.149	1.00	11.50			A	C
ANISOU	2291	CG2	VAL	A	557	1411	1344	1611	-21	0	-106		A	C
ATOM	2295	C	VAL	A	557	6.916	5.690	30.481	1.00	11.26			A	C
ANISOU	2295	C	VAL	A	557	1376	1443	1460	1	26	-82		A	C
ATOM	2296	O	VAL	A	557	7.056	6.887	30.794	1.00	11.64			A	O
ANISOU	2296	O	VAL	A	557	1282	1456	1684	73	-4	-146		A	O
ATOM	2297	N	ALA	A	558	5.872	4.974	30.860	1.00	12.16			A	N
ANISOU	2297	N	ALA	A	558	1549	1560	1509	-76	-6	-103		A	N
ATOM	2299	CA	ALA	A	558	4.879	5.498	31.793	1.00	12.50			A	C
ANISOU	2299	CA	ALA	A	558	1508	1649	1592	28	24	-50		A	C
ATOM	2301	CB	ALA	A	558	3.598	4.672	31.704	1.00	12.80			A	C
ANISOU	2301	CB	ALA	A	558	1634	1655	1573	-49	6	-47		A	C
ATOM	2305	C	ALA	A	558	5.390	5.485	33.238	1.00	12.51			A	C
ANISOU	2305	C	ALA	A	558	1535	1663	1552	47	-31	-122		A	C
ATOM	2306	O	ALA	A	558	5.104	6.380	34.066	1.00	14.27			A	O
ANISOU	2306	O	ALA	A	558	1703	1875	1841	126	-98	-181		A	O
ATOM	2307	N	SER	A	559	6.096	4.421	33.574	1.00	12.55			A	N
ANISOU	2307	N	SER	A	559	1564	1624	1580	5	-8	-68		A	N
ATOM	2309	CA	SER	A	559	6.722	4.284	34.883	1.00	12.69			A	C
ANISOU	2309	CA	SER	A	559	1603	1618	1599	-24	6	-60		A	C
ATOM	2311	CB	SER	A	559	5.695	3.793	35.901	1.00	12.95			A	C
ANISOU	2311	CB	SER	A	559	1673	1634	1613	9	34	1		A	C
ATOM	2314	OG	SER	A	559	5.391	2.428	35.687	1.00	14.31			A	O
ANISOU	2314	OG	SER	A	559	1859	1733	1843	0	192	-165		A	O
ATOM	2316	C	SER	A	559	7.828	3.264	34.747	1.00	12.56			A	C
ANISOU	2316	C	SER	A	559	1543	1639	1587	-22	51	-34		A	C
ATOM	2317	O	SER	A	559	7.885	2.580	33.719	1.00	12.75			A	O
ANISOU	2317	O	SER	A	559	1590	1693	1560	-111	69	-101		A	O
ATOM	2318	N	PRO	A	560	8.696	3.113	35.742	1.00	12.53			A	N
ANISOU	2318	N	PRO	A	560	1577	1600	1582	-19	21	-83		A	N
ATOM	2319	CA	PRO	A	560	9.684	2.019	35.688	1.00	13.14			A	C
ANISOU	2319	CA	PRO	A	560	1654	1704	1633	23	25	-36		A	C
ATOM	2321	CB	PRO	A	560	10.423	2.146	37.011	1.00	13.21			A	C

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ANISOU 2321  CB  PRO A 560     1593   1721   1705     46      0    -50  A    C
ATOM   2324  CG  PRO A 560      10.289   3.595  37.339  1.00 13.53       A    C
ANISOU 2324  CG  PRO A 560     1632   1733   1775    -64    -20    -70  A    C
ATOM   2327  CD  PRO A 560       8.892   3.966  36.929  1.00 13.11       A    C
ANISOU 2327  CD  PRO A 560     1688   1704   1586     63     -3    -27  A    C
ATOM   2330  C   PRO A 560       9.064   0.619  35.507  1.00 13.46       A    C
ANISOU 2330  C   PRO A 560     1734   1706   1674     25     26    -53  A    C
ATOM   2331  O   PRO A 560       9.781  -0.325  35.091  1.00 14.90       A    O
ANISOU 2331  O   PRO A 560     2001   1925   1736    102    149   -117  A    O
ATOM   2332  N   GLU A 561       7.764   0.499  35.784  1.00 14.34       A    N
ANISOU 2332  N   GLU A 561     1839   1877   1732     -8     27    -80  A    N
ATOM   2334  CA  GLU A 561       7.047  -0.771  35.718  1.00 14.84       A    C
ANISOU 2334  CA  GLU A 561     1929   1900   1809    -27     14    -57  A    C
ATOM   2336  CB  GLU A 561       6.041  -0.890  36.883  1.00 16.70       A    C
ANISOU 2336  CB  GLU A 561     2112   2109   2124   -109     61    -10  A    C
ATOM   2339  CG  GLU A 561       6.678  -0.972  38.251  1.00 20.63       A    C
ANISOU 2339  CG  GLU A 561     2661   2689   2487     -4    -55     25  A    C
ATOM   2342  CD  GLU A 561       7.188   0.367  38.748  1.00 25.39       A    C
ANISOU 2342  CD  GLU A 561     3275   3015   3357   -100    -42    -45  A    C
ATOM   2343  OE1 GLU A 561       6.484   1.405  38.583  1.00 27.09       A    O
ANISOU 2343  OE1 GLU A 561     3289   3365   3639     65    -24     69  A    O
ATOM   2344  OE2 GLU A 561       8.308   0.373  39.309  1.00 29.08       A    O
ANISOU 2344  OE2 GLU A 561     3480   3721   3845    -62   -156     52  A    O
ATOM   2345  C   GLU A 561       6.245  -0.953  34.440  1.00 13.68       A    C
ANISOU 2345  C   GLU A 561     1749   1762   1684    -21     39    -34  A    C
ATOM   2346  O   GLU A 561       5.624  -1.988  34.275  1.00 13.37       A    O
ANISOU 2346  O   GLU A 561     1859   1716   1503    -42     73   -194  A    O
ATOM   2347  N   CYS A 562       6.216   0.040  33.565  1.00 12.49       A    N
ANISOU 2347  N   CYS A 562     1594   1673   1479    -68     24    -56  A    N
ATOM   2349  CA  CYS A 562       5.275  -0.001  32.455  1.00 13.84       A    C
ANISOU 2349  CA  CYS A 562     1726   1863   1668    -17     34      0  A    C
ATOM   2351  CB  CYS A 562       3.902   0.495  32.925  1.00 14.48       A    C
ANISOU 2351  CB  CYS A 562     1810   1887   1802     -6     54    -57  A    C
ATOM   2354  SG  CYS A 562       2.661   0.449  31.631  1.00 17.07       A    S
ANISOU 2354  SG  CYS A 562     1661   2589   2234     89    144   -150  A    S
ATOM   2355  C   CYS A 562       5.703   0.831  31.253  1.00 12.03       A    C
ANISOU 2355  C   CYS A 562     1505   1592   1471    -22     53    -32  A    C
ATOM   2356  O   CYS A 562       5.878   2.048  31.345  1.00 11.76       A    O
ANISOU 2356  O   CYS A 562     1560   1728   1180    -40    142   -131  A    O
ATOM   2357  N   VAL A 563       5.829   0.158  30.111  1.00 11.30       A    N
ANISOU 2357  N   VAL A 563     1394   1522   1374     48     42    -32  A    N
ATOM   2359  CA  VAL A 563       6.071   0.838  28.857  1.00 10.98       A    C
ANISOU 2359  CA  VAL A 563     1335   1426   1408     30     54    -24  A    C
ATOM   2361  CB  VAL A 563       7.361   0.341  28.161  1.00 10.70       A    C
ANISOU 2361  CB  VAL A 563     1299   1395   1372     29     68     19  A    C
ATOM   2363  CG1 VAL A 563       8.574   0.604  29.051  1.00 11.76       A    C
ANISOU 2363  CG1 VAL A 563     1401   1449   1616     31    -27      0  A    C
ATOM   2367  CG2 VAL A 563       7.275  -1.143  27.774  1.00 11.15       A    C
ANISOU 2367  CG2 VAL A 563     1313   1418   1504    -63     72     19  A    C
ATOM   2371  C   VAL A 563       4.863   0.722  27.912  1.00 10.38       A    C
ANISOU 2371  C   VAL A 563     1292   1348   1303     42     89    -65  A    C
ATOM   2372  O   VAL A 563       4.009  -0.146  28.064  1.00 11.15       A    O
ANISOU 2372  O   VAL A 563     1408   1398   1430    -81     37   -177  A    O
ATOM   2373  N   LYS A 564       4.828   1.584  26.913  1.00 10.63       A    N
ANISOU 2373  N   LYS A 564     1296   1358   1384     95     76    -23  A    N
ATOM   2375  CA  LYS A 564       3.696   1.692  26.000  1.00 11.44       A    C
ANISOU 2375  CA  LYS A 564     1485   1469   1391     36    -19    -51  A    C
ATOM   2377  CB  LYS A 564       2.766   2.828  26.410  1.00 13.11       A    C
ANISOU 2377  CB  LYS A 564     1649   1790   1540    137     56     26  A    C
ATOM   2380  CG  LYS A 564       2.215   2.624  27.825  1.00 15.67       A    C
ANISOU 2380  CG  LYS A 564     2152   2218   1583    118    -24    -25  A    C
ATOM   2383  CD  LYS A 564       0.846   3.066  28.038  1.00 17.90       A    C
ANISOU 2383  CD  LYS A 564     2303   2192   2305      8     24    -23  A    C
ATOM   2386  CE  LYS A 564       0.585   3.113  29.531  1.00 18.28       A    C
ANISOU 2386  CE  LYS A 564     2360   2253   2331    158     81   -141  A    C
ATOM   2389  NZ  LYS A 564      -0.781   2.659  29.852  1.00 22.77       A    N
ANISOU 2389  NZ  LYS A 564     2792   3039   2819   -210    121    -24  A    N
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ATOM   2393  C   LYS A 564      4.172   1.938  24.591  1.00 10.77           A    C
ANISOU 2393  C   LYS A 564     1309   1375   1408     55     22    -16  A    C
ATOM   2394  O   LYS A 564      4.941   2.864  24.328  1.00 10.74           A    O
ANISOU 2394  O   LYS A 564     1239   1341   1500    120     52   -122  A    O
ATOM   2395  N   LEU A 565      3.730   1.079  23.689  1.00 10.25           A    N
ANISOU 2395  N   LEU A 565     1254   1252   1389     53     28    -25  A    N
ATOM   2397  CA  LEU A 565      4.035   1.227  22.285  1.00 10.59           A    C
ANISOU 2397  CA  LEU A 565     1364   1334   1322     36    -44     11  A    C
ATOM   2399  CB  LEU A 565      3.543  -0.003  21.533  1.00 11.06           A    C
ANISOU 2399  CB  LEU A 565     1495   1274   1430     23    -75     87  A    C
ATOM   2402  CG  LEU A 565      3.798  -0.071  20.038  1.00 12.33           A    C
ANISOU 2402  CG  LEU A 565     1649   1558   1476    100    -72    -66  A    C
ATOM   2404  CD1 LEU A 565      5.275  -0.056  19.762  1.00 13.31           A    C
ANISOU 2404  CD1 LEU A 565     1811   1742   1501    103     88    -47  A    C
ATOM   2408  CD2 LEU A 565      3.139  -1.293  19.470  1.00 13.66           A    C
ANISOU 2408  CD2 LEU A 565     1947   1735   1509     56   -141     58  A    C
ATOM   2412  C   LEU A 565      3.378   2.475  21.718  1.00 11.22           A    C
ANISOU 2412  C   LEU A 565     1427   1366   1468     56     20    -44  A    C
ATOM   2413  O   LEU A 565      2.191   2.721  21.937  1.00 11.52           A    O
ANISOU 2413  O   LEU A 565     1372   1402   1603    214    113    -16  A    O
ATOM   2414  N   GLY A 566      4.140   3.232  20.942  1.00 12.46           A    N
ANISOU 2414  N   GLY A 566     1579   1574   1578     46     -6    -14  A    N
ATOM   2416  CA  GLY A 566      3.628   4.441  20.315  1.00 13.36           A    C
ANISOU 2416  CA  GLY A 566     1744   1575   1756     50     45     14  A    C
ATOM   2419  C   GLY A 566      2.830   4.241  19.038  1.00 15.83           A    C
ANISOU 2419  C   GLY A 566     1988   2012   2015     36      5    -17  A    C
ATOM   2420  O   GLY A 566      2.460   3.136  18.671  1.00 15.30           A    O
ANISOU 2420  O   GLY A 566     1818   1989   2003    230     -5     24  A    O
ATOM   2421  N   ASP A 567      2.610   5.366  18.358  1.00 18.88           A    N
ANISOU 2421  N   ASP A 567     2485   2299   2388    120    -17     26  A    N
ATOM   2423  CA  ASP A 567      1.821   5.454  17.123  1.00 22.18           A    C
ANISOU 2423  CA  ASP A 567     2820   2815   2790     34    -77     10  A    C
ATOM   2425  CB  ASP A 567      1.743   6.909  16.652  1.00 23.80           A    C
ANISOU 2425  CB  ASP A 567     3063   3001   2978     85    -85     46  A    C
ATOM   2428  CG  ASP A 567      1.123   7.810  17.647  1.00 27.77           A    C
ANISOU 2428  CG  ASP A 567     3596   3515   3436     94     -1    -93  A    C
ATOM   2429  OD1 ASP A 567      0.351   7.324  18.502  1.00 31.50           A    O
ANISOU 2429  OD1 ASP A 567     3849   4126   3993   -103    119     59  A    O
ATOM   2430  OD2 ASP A 567      1.370   9.031  17.647  1.00 32.32           A    O
ANISOU 2430  OD2 ASP A 567     4227   3735   4317   -132    -17      8  A    O
ATOM   2431  C   ASP A 567      2.407   4.717  15.954  1.00 23.94           A    C
ANISOU 2431  C   ASP A 567     3056   3019   3019     49     15     21  A    C
ATOM   2432  O   ASP A 567      3.570   4.375  15.926  1.00 20.99           A    O
ANISOU 2432  O   ASP A 567     2719   2583   2671     42   -104    189  A    O
ATOM   2433  N   PHE A 568      1.581   4.572  14.934  1.00 27.78           A    N
ANISOU 2433  N   PHE A 568     3437   3614   3502     58   -107      0  A    N
ATOM   2435  CA  PHE A 568      1.940   3.852  13.718  1.00 31.07           A    C
ANISOU 2435  CA  PHE A 568     3939   3981   3883     45    -33    -57  A    C
ATOM   2437  CB  PHE A 568      0.690   3.615  12.890  1.00 31.44           A    C
ANISOU 2437  CB  PHE A 568     4014   4000   3932     35    -50     -2  A    C
ATOM   2440  CG  PHE A 568     -0.310   2.813  13.602  1.00 32.10           A    C
ANISOU 2440  CG  PHE A 568     4049   4112   4033    -49      8    -29  A    C
ATOM   2441  CD1 PHE A 568     -0.090   1.468  13.790  1.00 33.05           A    C
ANISOU 2441  CD1 PHE A 568     4152   4222   4181     78      8      6  A    C
ATOM   2443  CE1 PHE A 568     -0.992   0.699  14.489  1.00 33.55           A    C
ANISOU 2443  CE1 PHE A 568     4179   4250   4319      4    -26     53  A    C
ATOM   2445  CZ  PHE A 568     -2.118   1.290  15.038  1.00 33.51           A    C
ANISOU 2445  CZ  PHE A 568     4275   4211   4243      6     34      1  A    C
ATOM   2447  CE2 PHE A 568     -2.335   2.650  14.866  1.00 33.37           A    C
ANISOU 2447  CE2 PHE A 568     4194   4249   4234      6      6    -25  A    C
ATOM   2449  CD2 PHE A 568     -1.431   3.403  14.167  1.00 32.67           A    C
ANISOU 2449  CD2 PHE A 568     4165   4077   4172     31      1    -30  A    C
ATOM   2451  C   PHE A 568      2.952   4.572  12.891  1.00 34.06           A    C
ANISOU 2451  C   PHE A 568     4336   4339   4266    -22    -41     24  A    C
ATOM   2452  O   PHE A 568      3.100   5.787  12.998  1.00 34.68           A    O
ANISOU 2452  O   PHE A 568     4525   4338   4311     59    -28    -26  A    O
ATOM   2453  N   GLY A 569      3.653   3.800  12.061  1.00 37.04           A    N
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ANISOU 2453  N   GLY A 569     4697   4714   4661     48    -34    -63  A    N
ATOM   2455  CA  GLY A 569       4.677   4.325  11.180  1.00 39.68       A    C
ANISOU 2455  CA  GLY A 569     5005   5045   5025    -14     29      0  A    C
ATOM   2458  C   GLY A 569       4.199   4.680   9.781  1.00 42.00       A    C
ANISOU 2458  C   GLY A 569     5343   5348   5265     12     -8      9  A    C
ATOM   2459  O   GLY A 569       5.017   5.059   8.933  1.00 42.55       A    O
ANISOU 2459  O   GLY A 569     5375   5396   5396    -26     54     23  A    O
ATOM   2460  N   LEU A 570       2.890   4.581   9.533  1.00 44.32       A    N
ANISOU 2460  N   LEU A 570     5557   5638   5644     -8      2     -7  A    N
ATOM   2462  CA  LEU A 570       2.346   4.764   8.172  1.00 46.07       A    C
ANISOU 2462  CA  LEU A 570     5828   5864   5810      2    -10      0  A    C
ATOM   2464  CB  LEU A 570       0.892   4.250   8.042  1.00 46.30       A    C
ANISOU 2464  CB  LEU A 570     5844   5877   5871      0    -20      0  A    C
ATOM   2467  CG  LEU A 570      -0.034   4.052   9.255  1.00 46.98       A    C
ANISOU 2467  CG  LEU A 570     5939   5964   5945      1      4      2  A    C
ATOM   2469  CD1 LEU A 570      -0.765   5.343   9.594  1.00 47.51       A    C
ANISOU 2469  CD1 LEU A 570     6012   6000   6039     10      5    -15  A    C
ATOM   2473  CD2 LEU A 570      -1.032   2.924   9.007  1.00 47.32       A    C
ANISOU 2473  CD2 LEU A 570     5977   5970   6030     -7      6     -8  A    C
ATOM   2477  C   LEU A 570       2.470   6.210   7.655  1.00 47.30       A    C
ANISOU 2477  C   LEU A 570     5999   5969   6004     -5      0     -1  A    C
ATOM   2478  O   LEU A 570       2.024   7.158   8.300  1.00 47.60       A    O
ANISOU 2478  O   LEU A 570     6036   6001   6049      6      1    -27  A    O
ATOM   2479  N   SER A 571       3.064   6.343   6.467  1.00 48.73       A    N
ANISOU 2479  N   SER A 571     6175   6189   6151    -14      9      6  A    N
ATOM   2481  CA  SER A 571       3.477   7.633   5.893  1.00 49.54       A    C
ANISOU 2481  CA  SER A 571     6285   6262   6275     -9      3     14  A    C
ATOM   2483  CB  SER A 571       4.172   7.412   4.535  1.00 49.55       A    C
ANISOU 2483  CB  SER A 571     6270   6281   6276      3      4     18  A    C
ATOM   2486  OG  SER A 571       5.577   7.560   4.643  1.00 49.55       A    O
ANISOU 2486  OG  SER A 571     6267   6278   6279    -13      8     35  A    O
ATOM   2488  C   SER A 571       2.342   8.637   5.707  1.00 50.18       A    C
ANISOU 2488  C   SER A 571     6344   6361   6360     12      6      0  A    C
ATOM   2489  O   SER A 571       1.164   8.282   5.771  1.00 50.60       A    O
ANISOU 2489  O   SER A 571     6400   6405   6419    -16     15     -8  A    O
ATOM   2490  N   ARG A 572       2.727   9.887   5.452  1.00 50.82       A    N
ANISOU 2490  N   ARG A 572     6440   6420   6447     -5      6      0  A    N
ATOM   2492  CA  ARG A 572       1.783  10.990   5.235  1.00 51.28       A    C
ANISOU 2492  CA  ARG A 572     6492   6494   6497      5      1      1  A    C
ATOM   2494  CB  ARG A 572       1.830  11.971   6.419  1.00 51.64       A    C
ANISOU 2494  CB  ARG A 572     6547   6531   6542      6      7    -11  A    C
ATOM   2497  CG  ARG A 572       3.205  12.606   6.691  1.00 52.82       A    C
ANISOU 2497  CG  ARG A 572     6657   6714   6695    -19     -6     -9  A    C
ATOM   2500  CD  ARG A 572       3.285  14.116   6.426  1.00 54.29       A    C
ANISOU 2500  CD  ARG A 572     6915   6823   6886      5      5     10  A    C
ATOM   2503  NE  ARG A 572       4.593  14.668   6.793  1.00 55.46       A    N
ANISOU 2503  NE  ARG A 572     6988   7037   7045    -22    -19     -6  A    N
ATOM   2505  CZ  ARG A 572       4.888  15.968   6.845  1.00 56.06       A    C
ANISOU 2505  CZ  ARG A 572     7109   7064   7125     -8     -2      5  A    C
ATOM   2506  NH1 ARG A 572       3.977  16.889   6.550  1.00 56.24       A    N
ANISOU 2506  NH1 ARG A 572     7113   7117   7136      6     -2     14  A    N
ATOM   2509  NH2 ARG A 572       6.112  16.351   7.195  1.00 56.51       A    N
ANISOU 2509  NH2 ARG A 572     7136   7146   7188     -5    -10    -12  A    N
ATOM   2512  C   ARG A 572       2.055  11.723   3.912  1.00 51.09       A    C
ANISOU 2512  C   ARG A 572     6476   6470   6466      6      3     -5  A    C
ATOM   2513  O   ARG A 572       1.921  12.950   3.829  1.00 51.39       A    O
ANISOU 2513  O   ARG A 572     6504   6510   6509     10      2    -17  A    O
ATOM   2514  N   TYR A 573       2.419  10.960   2.879  1.00 50.77       A    N
ANISOU 2514  N   TYR A 573     6439   6431   6418      1     -1      3  A    N
ATOM   2516  CA  TYR A 573       2.760  11.514   1.563  1.00 50.38       A    C
ANISOU 2516  CA  TYR A 573     6391   6380   6369     -2     -8     -5  A    C
ATOM   2518  CB  TYR A 573       4.283  11.462   1.352  1.00 50.71       A    C
ANISOU 2518  CB  TYR A 573     6417   6430   6420      1     -3     -3  A    C
ATOM   2521  CG  TYR A 573       4.830  12.554   0.449  1.00 51.77       A    C
ANISOU 2521  CG  TYR A 573     6570   6547   6551    -15      5     22  A    C
ATOM   2522  CD1 TYR A 573       5.530  12.242  -0.721  1.00 52.38       A    C
ANISOU 2522  CD1 TYR A 573     6632   6648   6622      5     25      0  A    C
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ATOM   2524  CE1 TYR A 573       6.028  13.246  -1.552  1.00 52.54           A    C
ANISOU 2524  CE1 TYR A 573    6645   6649   6668    -11      15     10  A    C
ATOM   2526  CZ  TYR A 573       5.830  14.577  -1.214  1.00 52.84           A    C
ANISOU 2526  CZ  TYR A 573    6692   6687   6695     -5      15     -8  A    C
ATOM   2527  OH  TYR A 573       6.316  15.580  -2.026  1.00 52.93           A    O
ANISOU 2527  OH  TYR A 573    6703   6694   6713    -15      15      3  A    O
ATOM   2529  CE2 TYR A 573       5.141  14.909  -0.059  1.00 52.70           A    C
ANISOU 2529  CE2 TYR A 573    6675   6668   6679    -18      12      4  A    C
ATOM   2531  CD2 TYR A 573       4.649  13.900   0.765  1.00 52.48           A    C
ANISOU 2531  CD2 TYR A 573    6667   6613   6658      6       2    -12  A    C
ATOM   2533  C   TYR A 573       2.034  10.761   0.433  1.00 49.50           A    C
ANISOU 2533  C   TYR A 573    6292   6261   6253      0      -2     18  A    C
ATOM   2534  O   TYR A 573       1.740   9.566   0.562  1.00 49.79           A    O
ANISOU 2534  O   TYR A 573    6333   6284   6301    -18      -1     -4  A    O
ATOM   2535  N   ILE A 574       1.751  11.472  -0.665  1.00 48.15           A    N
ANISOU 2535  N   ILE A 574    6101   6097   6096     -7     -17    -21  A    N
ATOM   2537  CA  ILE A 574       1.032  10.906  -1.820  1.00 46.82           A    C
ANISOU 2537  CA  ILE A 574    5931   5911   5946     12      11     -6  A    C
ATOM   2539  CB  ILE A 574       0.824  11.987  -2.966  1.00 47.04           A    C
ANISOU 2539  CB  ILE A 574    5958   5953   5959     -3       2     -3  A    C
ATOM   2541  CG1 ILE A 574       0.115  11.378  -4.188  1.00 47.21           A    C
ANISOU 2541  CG1 ILE A 574    5979   5977   5980      4      -9     -6  A    C
ATOM   2544  CD1 ILE A 574      -0.113  12.358  -5.328  1.00 47.28           A    C
ANISOU 2544  CD1 ILE A 574    5982   5982   6001     15       2     10  A    C
ATOM   2548  CG2 ILE A 574       2.144  12.663  -3.400  1.00 47.22           A    C
ANISOU 2548  CG2 ILE A 574    5967   5985   5987     -4      11     -8  A    C
ATOM   2552  C   ILE A 574       1.659   9.607  -2.367  1.00 45.25           A    C
ANISOU 2552  C   ILE A 574    5692   5756   5745    -17      24      4  A    C
ATOM   2553  O   ILE A 574       1.095   8.513  -2.190  1.00 45.46           A    O
ANISOU 2553  O   ILE A 574    5743   5753   5777    -15      14      3  A    O
ATOM   2554  N   GLU A 575       2.832   9.717  -2.989  1.00 42.99           A    N
ANISOU 2554  N   GLU A 575    5468   5415   5448      6       5    -23  A    N
ATOM   2556  CA  GLU A 575       3.425   8.595  -3.722  1.00 40.89           A    C
ANISOU 2556  CA  GLU A 575    5189   5163   5184      0      -5     26  A    C
ATOM   2558  CB  GLU A 575       4.684   9.041  -4.489  1.00 41.19           A    C
ANISOU 2558  CB  GLU A 575    5209   5210   5230      4      12      4  A    C
ATOM   2561  CG  GLU A 575       4.416   9.455  -5.931  1.00 42.08           A    C
ANISOU 2561  CG  GLU A 575    5364   5308   5315      6     -12      5  A    C
ATOM   2564  CD  GLU A 575       5.674   9.887  -6.668  1.00 43.35           A    C
ANISOU 2564  CD  GLU A 575    5470   5494   5507     -6      35     13  A    C
ATOM   2565  OE1 GLU A 575       6.746   9.274  -6.448  1.00 43.91           A    O
ANISOU 2565  OE1 GLU A 575    5551   5535   5596     35     -28     40  A    O
ATOM   2566  OE2 GLU A 575       5.590  10.844  -7.476  1.00 44.09           A    O
ANISOU 2566  OE2 GLU A 575    5633   5563   5553     11      -1     40  A    O
ATOM   2567  C   GLU A 575       3.737   7.367  -2.853  1.00 38.22           A    C
ANISOU 2567  C   GLU A 575    4849   4868   4803     -3      -7    -34  A    C
ATOM   2568  O   GLU A 575       3.833   6.259  -3.397  1.00 38.54           A    O
ANISOU 2568  O   GLU A 575    4862   4870   4909     11      -1    -16  A    O
ATOM   2569  N   ASP A 576       3.894   7.574  -1.534  1.00 34.64           A    N
ANISOU 2569  N   ASP A 576    4378   4342   4440     16      15     34  A    N
ATOM   2571  CA  ASP A 576       4.123   6.525  -0.520  1.00 31.46           A    C
ANISOU 2571  CA  ASP A 576    3940   3975   4038     49      17    -35  A    C
ATOM   2573  CB  ASP A 576       2.798   5.899  -0.068  1.00 31.90           A    C
ANISOU 2573  CB  ASP A 576    4039   3982   4099     11      21     18  A    C
ATOM   2576  CG  ASP A 576       2.962   4.913   1.094  1.00 32.79           A    C
ANISOU 2576  CG  ASP A 576    4172   4136   4151     46       9     10  A    C
ATOM   2577  OD1 ASP A 576       3.073   3.705   0.828  1.00 30.61           A    O
ANISOU 2577  OD1 ASP A 576    3905   3925   3798     24      40     -7  A    O
ATOM   2578  OD2 ASP A 576       2.943   5.232   2.306  1.00 36.41           A    O
ANISOU 2578  OD2 ASP A 576    4694   4671   4466     27     -10   -129  A    O
ATOM   2579  C   ASP A 576       5.135   5.445  -0.921  1.00 27.81           A    C
ANISOU 2579  C   ASP A 576    3527   3515   3523     -2     -36     26  A    C
ATOM   2580  O   ASP A 576       5.102   4.917  -2.026  1.00 26.13           A    O
ANISOU 2580  O   ASP A 576    3282   3194   3451     36     -28     40  A    O
ATOM   2581  N   GLU A 577       6.030   5.127   0.006  1.00 24.06           A    N
ANISOU 2581  N   GLU A 577    3046   3003   3090     24      47    -22  A    N
ATOM   2583  CA  GLU A 577       7.183   4.284  -0.294  1.00 21.31           A    C
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ANISOU 2583  CA  GLU A 577     2749   2641   2704    -29     -1     13  A    C
ATOM   2585  CB  GLU A 577       8.290   4.492   0.743  1.00 21.05      A    C
ANISOU 2585  CB  GLU A 577     2716   2636   2645      8     30     15  A    C
ATOM   2588  CG  GLU A 577       8.936   5.867   0.652  1.00 22.39      A    C
ANISOU 2588  CG  GLU A 577     2889   2763   2855    -53     -6    -43  A    C
ATOM   2591  CD  GLU A 577      10.323   5.932   1.267  1.00 23.68      A    C
ANISOU 2591  CD  GLU A 577     2991   3002   3004     31    -25     42  A    C
ATOM   2592  OE1 GLU A 577      11.175   5.095   0.933  1.00 22.74      A    O
ANISOU 2592  OE1 GLU A 577     2823   2940   2876    -98     27     85  A    O
ATOM   2593  OE2 GLU A 577      10.557   6.839   2.088  1.00 26.39      A    O
ANISOU 2593  OE2 GLU A 577     3441   3169   3418    -40   -106    -30  A    O
ATOM   2594  C   GLU A 577       6.844   2.799  -0.430  1.00 19.18      A    C
ANISOU 2594  C   GLU A 577     2438   2448   2401    -10      3     39  A    C
ATOM   2595  O   GLU A 577       7.743   2.010  -0.666  1.00 18.10      A    O
ANISOU 2595  O   GLU A 577     2407   2158   2312    -54    -14     67  A    O
ATOM   2596  N   ASP A 578       5.564   2.425  -0.324  1.00 17.39      A    N
ANISOU 2596  N   ASP A 578     2240   2225   2140     21    -15     16  A    N
ATOM   2598  CA  ASP A 578       5.142   1.064  -0.671  1.00 16.41      A    C
ANISOU 2598  CA  ASP A 578     2082   2110   2040     10      0     22  A    C
ATOM   2600  CB  ASP A 578       3.747   0.728  -0.108  1.00 16.70      A    C
ANISOU 2600  CB  ASP A 578     2102   2185   2056     23    -22      5  A    C
ATOM   2603  CG  ASP A 578       3.721   0.575   1.396  1.00 17.80      A    C
ANISOU 2603  CG  ASP A 578     2269   2283   2210    -25      4     73  A    C
ATOM   2604  OD1 ASP A 578       4.744   0.836   2.080  1.00 18.44      A    O
ANISOU 2604  OD1 ASP A 578     2460   2283   2260     33    -34     46  A    O
ATOM   2605  OD2 ASP A 578       2.673   0.168   1.958  1.00 19.32      A    O
ANISOU 2605  OD2 ASP A 578     2556   2804   1980     25    129    191  A    O
ATOM   2606  C   ASP A 578       5.101   0.850  -2.194  1.00 15.80      A    C
ANISOU 2606  C   ASP A 578     2021   1999   1983     25     12      1  A    C
ATOM   2607  O   ASP A 578       4.982  -0.283  -2.661  1.00 15.16      A    O
ANISOU 2607  O   ASP A 578     1934   2018   1806     66     29    -29  A    O
ATOM   2608  N   TYR A 579       5.154   1.942  -2.947  1.00 15.54      A    N
ANISOU 2608  N   TYR A 579     1978   1989   1934    -25     22      0  A    N
ATOM   2610  CA  TYR A 579       4.949   1.919  -4.396  1.00 15.86      A    C
ANISOU 2610  CA  TYR A 579     2010   2019   1994     16    -14     20  A    C
ATOM   2612  CB  TYR A 579       3.878   2.949  -4.751  1.00 15.76      A    C
ANISOU 2612  CB  TYR A 579     2011   1982   1992      6      3     45  A    C
ATOM   2615  CG  TYR A 579       2.527   2.607  -4.227  1.00 16.35      A    C
ANISOU 2615  CG  TYR A 579     2024   2045   2141     67      1     17  A    C
ATOM   2616  CD1 TYR A 579       1.619   1.912  -5.010  1.00 17.24      A    C
ANISOU 2616  CD1 TYR A 579     2203   2167   2179     47    -51     -9  A    C
ATOM   2618  CE1 TYR A 579       0.367   1.573  -4.526  1.00 18.73      A    C
ANISOU 2618  CE1 TYR A 579     2353   2364   2399    -10    -14     23  A    C
ATOM   2620  CZ  TYR A 579      -0.002   1.946  -3.259  1.00 19.96      A    C
ANISOU 2620  CZ  TYR A 579     2495   2490   2596     45     50    -42  A    C
ATOM   2621  OH  TYR A 579      -1.257   1.594  -2.806  1.00 23.30      A    O
ANISOU 2621  OH  TYR A 579     2638   3008   3204     -9    164    -76  A    O
ATOM   2623  CE2 TYR A 579       0.876   2.636  -2.453  1.00 19.53      A    C
ANISOU 2623  CE2 TYR A 579     2459   2491   2469     42     95    -66  A    C
ATOM   2625  CD2 TYR A 579       2.149   2.962  -2.936  1.00 18.93      A    C
ANISOU 2625  CD2 TYR A 579     2448   2411   2333     -3     12    -65  A    C
ATOM   2627  C   TYR A 579       6.214   2.199  -5.206  1.00 16.65      A    C
ANISOU 2627  C   TYR A 579     2123   2109   2091     30      8      2  A    C
ATOM   2628  O   TYR A 579       6.240   1.995  -6.419  1.00 17.08      A    O
ANISOU 2628  O   TYR A 579     2170   2171   2148      4      7     12  A    O
ATOM   2629  N   TYR A 580       7.257   2.676  -4.538  1.00 17.48      A    N
ANISOU 2629  N   TYR A 580     2180   2208   2254     12     13    -20  A    N
ATOM   2631  CA  TYR A 580       8.512   3.024  -5.197  1.00 17.86      A    C
ANISOU 2631  CA  TYR A 580     2242   2256   2285     -1     37     -5  A    C
ATOM   2633  CB  TYR A 580       8.451   4.465  -5.766  1.00 18.09      A    C
ANISOU 2633  CB  TYR A 580     2274   2296   2302     -8     22     35  A    C
ATOM   2636  CG  TYR A 580       8.481   5.556  -4.709  1.00 18.48      A    C
ANISOU 2636  CG  TYR A 580     2326   2301   2392    -21     15      0  A    C
ATOM   2637  CD1 TYR A 580       9.689   6.102  -4.268  1.00 17.63      A    C
ANISOU 2637  CD1 TYR A 580     2232   2214   2252     18     33     99  A    C
ATOM   2639  CE1 TYR A 580       9.729   7.072  -3.300  1.00 18.28      A    C
ANISOU 2639  CE1 TYR A 580     2343   2148   2453    -45     47     77  A    C
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ATOM   2641  CZ  TYR A 580       8.549   7.547  -2.745  1.00 19.74           A    C
ANISOU 2641  CZ  TYR A 580    2440   2514   2544    -11     20     51  A    C
ATOM   2642  OH  TYR A 580       8.594   8.526  -1.776  1.00 21.33           A    O
ANISOU 2642  OH  TYR A 580    2750   2415   2937   -128     50     68  A    O
ATOM   2644  CE2 TYR A 580       7.326   7.024  -3.158  1.00 20.10           A    C
ANISOU 2644  CE2 TYR A 580    2490   2505   2639    -21     38    -24  A    C
ATOM   2646  CD2 TYR A 580       7.300   6.041  -4.143  1.00 18.84           A    C
ANISOU 2646  CD2 TYR A 580    2334   2379   2446    -16     19     40  A    C
ATOM   2648  C   TYR A 580       9.713   2.848  -4.271  1.00 17.89           A    C
ANISOU 2648  C   TYR A 580    2269   2274   2253    -32     32    -16  A    C
ATOM   2649  O   TYR A 580       9.600   2.942  -3.030  1.00 17.99           A    O
ANISOU 2649  O   TYR A 580    2292   2255   2288    -54    105      5  A    O
ATOM   2650  N   LYS A 581      10.863   2.584  -4.893  1.00 18.02           A    N
ANISOU 2650  N   LYS A 581    2255   2257   2333      4      1      0  A    N
ATOM   2652  CA  LYS A 581      12.136   2.505  -4.201  1.00 17.79           A    C
ANISOU 2652  CA  LYS A 581    2238   2225   2297    -19     13    -19  A    C
ATOM   2654  CB  LYS A 581      13.032   1.431  -4.820  1.00 18.41           A    C
ANISOU 2654  CB  LYS A 581    2290   2298   2406     13      6    -25  A    C
ATOM   2657  CG  LYS A 581      12.516   0.033  -4.640  1.00 19.43           A    C
ANISOU 2657  CG  LYS A 581    2453   2376   2553    -12      7    -17  A    C
ATOM   2660  CD  LYS A 581      12.368  -0.307  -3.177  1.00 20.34           A    C
ANISOU 2660  CD  LYS A 581    2563   2558   2605     14    -29      1  A    C
ATOM   2663  CE  LYS A 581      12.436  -1.810  -2.931  1.00 20.07           A    C
ANISOU 2663  CE  LYS A 581    2521   2484   2619     -2     14     -8  A    C
ATOM   2666  NZ  LYS A 581      13.759  -2.435  -3.299  1.00 21.13           A    N
ANISOU 2666  NZ  LYS A 581    2474   2729   2823    -12     42    -38  A    N
ATOM   2670  C   LYS A 581      12.818   3.853  -4.316  1.00 16.99           A    C
ANISOU 2670  C   LYS A 581    2141   2142   2172     -8     36     30  A    C
ATOM   2671  O   LYS A 581      13.245   4.263  -5.413  1.00 18.03           A    O
ANISOU 2671  O   LYS A 581    2308   2234   2309     25     84     38  A    O
ATOM   2672  N   ALA A 582      12.902   4.536  -3.183  1.00 15.82           A    N
ANISOU 2672  N   ALA A 582    1955   1993   2060    -33     45     46  A    N
ATOM   2674  CA  ALA A 582      13.586   5.810  -3.082  1.00 15.68           A    C
ANISOU 2674  CA  ALA A 582    1978   1922   2058      0     23     38  A    C
ATOM   2676  CB  ALA A 582      13.321   6.444  -1.738  1.00 15.15           A    C
ANISOU 2676  CB  ALA A 582    1912   1910   1931     -7      8    103  A    C
ATOM   2680  C   ALA A 582      15.083   5.632  -3.284  1.00 16.35           A    C
ANISOU 2680  C   ALA A 582    2012   1998   2201      8     22     50  A    C
ATOM   2681  O   ALA A 582      15.623   4.587  -2.984  1.00 16.94           A    O
ANISOU 2681  O   ALA A 582    2032   1912   2491     11     50    104  A    O
ATOM   2682  N   SER A 583      15.753   6.661  -3.796  1.00 16.37           A    N
ANISOU 2682  N   SER A 583    2060   2003   2157      0     39     73  A    N
ATOM   2684  CA  SER A 583      17.217   6.677  -3.778  1.00 16.93           A    C
ANISOU 2684  CA  SER A 583    2104   2085   2240     23      4     34  A    C
ATOM   2686  CB  SER A 583      17.775   7.902  -4.502  1.00 16.51           A    C
ANISOU 2686  CB  SER A 583    2019   2086   2168     -2     44      4  A    C
ATOM   2689  OG  SER A 583      17.566   7.822  -5.897  1.00 14.11           A    O
ANISOU 2689  OG  SER A 583    1605   1680   2076     52    -26    -26  A    O
ATOM   2691  C   SER A 583      17.735   6.681  -2.346  1.00 17.70           A    C
ANISOU 2691  C   SER A 583    2243   2193   2287     10     10     67  A    C
ATOM   2692  O   SER A 583      18.697   5.982  -2.032  1.00 18.66           A    O
ANISOU 2692  O   SER A 583    2279   2288   2523     70    -14    112  A    O
ATOM   2693  N   VAL A 584      17.120   7.501  -1.498  1.00 18.19           A    N
ANISOU 2693  N   VAL A 584    2287   2261   2361     -5     29     56  A    N
ATOM   2695  CA  VAL A 584      17.413   7.556  -0.072  1.00 19.05           A    C
ANISOU 2695  CA  VAL A 584    2409   2408   2420    -25     29     40  A    C
ATOM   2697  CB  VAL A 584      18.096   8.871   0.357  1.00 19.66           A    C
ANISOU 2697  CB  VAL A 584    2511   2473   2485     -4     -4     10  A    C
ATOM   2699  CG1 VAL A 584      18.341   8.890   1.867  1.00 20.62           A    C
ANISOU 2699  CG1 VAL A 584    2665   2634   2532     -7    -23     -5  A    C
ATOM   2703  CG2 VAL A 584      19.381   9.060  -0.379  1.00 20.53           A    C
ANISOU 2703  CG2 VAL A 584    2621   2609   2567    -47     31     11  A    C
ATOM   2707  C   VAL A 584      16.078   7.449   0.648  1.00 18.95           A    C
ANISOU 2707  C   VAL A 584    2381   2398   2418    -23     59     51  A    C
ATOM   2708  O   VAL A 584      15.291   8.391   0.672  1.00 17.84           A    O
ANISOU 2708  O   VAL A 584    2262   2271   2245   -157    161    219  A    O
ATOM   2709  N   THR A 585      15.818   6.283   1.216  1.00 19.63           A    N
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ANISOU 2709  N   THR A 585     2483   2451   2523      0     34     58  A    N
ATOM   2711  CA  THR A 585      14.560   6.052   1.900  1.00 20.45         A    C
ANISOU 2711  CA  THR A 585     2574   2605   2590    -10     24     71  A    C
ATOM   2713  CB  THR A 585      14.287   4.549   2.007  1.00 21.03         A    C
ANISOU 2713  CB  THR A 585     2630   2664   2696      0    -24     12  A    C
ATOM   2715  OG1 THR A 585      12.964   4.321   2.525  1.00 21.93         A    O
ANISOU 2715  OG1 THR A 585     2848   2884   2600   -100    150    177  A    O
ATOM   2717  CG2 THR A 585      15.209   3.897   3.026  1.00 21.35         A    C
ANISOU 2717  CG2 THR A 585     2765   2668   2676      7    -40     96  A    C
ATOM   2721  C   THR A 585      14.512   6.709   3.281  1.00 20.98         A    C
ANISOU 2721  C   THR A 585     2671   2624   2676    -26     17     66  A    C
ATOM   2722  O   THR A 585      15.531   6.921   3.928  1.00 21.27         A    O
ANISOU 2722  O   THR A 585     2738   2558   2785   -153     35    137  A    O
ATOM   2723  N   ARG A 586      13.289   6.983   3.732  1.00 21.82         A    N
ANISOU 2723  N   ARG A 586     2782   2761   2745     31     47     43  A    N
ATOM   2725  CA  ARG A 586      13.031   7.549   5.052  1.00 21.86         A    C
ANISOU 2725  CA  ARG A 586     2852   2719   2735    -10     58     63  A    C
ATOM   2727  CB  ARG A 586      11.813   8.473   4.979  1.00 23.02         A    C
ANISOU 2727  CB  ARG A 586     2935   2927   2883      4     38      5  A    C
ATOM   2730  CG  ARG A 586      11.881   9.569   3.912  1.00 26.16         A    C
ANISOU 2730  CG  ARG A 586     3295   3342   3302     -3     15    126  A    C
ATOM   2733  CD  ARG A 586      11.676  10.988   4.464  1.00 30.42         A    C
ANISOU 2733  CD  ARG A 586     3912   3704   3939     10    -21    -49  A    C
ATOM   2736  NE  ARG A 586      10.804  11.017   5.645  1.00 33.93         A    N
ANISOU 2736  NE  ARG A 586     4286   4331   4274      6     80     35  A    N
ATOM   2738  CZ  ARG A 586      10.848  11.935   6.613  1.00 36.28         A    C
ANISOU 2738  CZ  ARG A 586     4628   4593   4562      5     -4    -70  A    C
ATOM   2739  NH1 ARG A 586      11.701  12.953   6.563  1.00 37.52         A    N
ANISOU 2739  NH1 ARG A 586     4744   4718   4792    -25      8     -2  A    N
ATOM   2742  NH2 ARG A 586      10.010  11.845   7.639  1.00 37.48         A    N
ANISOU 2742  NH2 ARG A 586     4743   4840   4655    -18     32      2  A    N
ATOM   2745  C   ARG A 586      12.743   6.405   6.040  1.00 20.86         A    C
ANISOU 2745  C   ARG A 586     2704   2585   2636    -11     41     41  A    C
ATOM   2746  O   ARG A 586      12.667   6.611   7.255  1.00 21.59         A    O
ANISOU 2746  O   ARG A 586     2933   2538   2732     11    112     56  A    O
ATOM   2747  N   LEU A 587      12.581   5.215   5.483  1.00 18.66         A    N
ANISOU 2747  N   LEU A 587     2390   2310   2388      8     81    121  A    N
ATOM   2749  CA  LEU A 587      12.161   4.031   6.232  1.00 17.34         A    C
ANISOU 2749  CA  LEU A 587     2176   2186   2226     -5     40    118  A    C
ATOM   2751  CB  LEU A 587      11.754   2.929   5.269  1.00 17.67         A    C
ANISOU 2751  CB  LEU A 587     2233   2283   2195     35     75     82  A    C
ATOM   2754  CG  LEU A 587      10.543   3.200   4.382  1.00 19.24         A    C
ANISOU 2754  CG  LEU A 587     2414   2472   2422    -25    -27    102  A    C
ATOM   2756  CD1 LEU A 587      10.419   2.131   3.317  1.00 21.02         A    C
ANISOU 2756  CD1 LEU A 587     2726   2638   2621     61    -25     59  A    C
ATOM   2760  CD2 LEU A 587       9.293   3.265   5.247  1.00 21.78         A    C
ANISOU 2760  CD2 LEU A 587     2677   2875   2721     26     34    -31  A    C
ATOM   2764  C   LEU A 587      13.279   3.522   7.136  1.00 15.98         A    C
ANISOU 2764  C   LEU A 587     1981   1985   2104      8     53    106  A    C
ATOM   2765  O   LEU A 587      14.474   3.747   6.860  1.00 15.60         A    O
ANISOU 2765  O   LEU A 587     1918   1860   2148     24     18    215  A    O
ATOM   2766  N   PRO A 588      12.896   2.852   8.224  1.00 14.09         A    N
ANISOU 2766  N   PRO A 588     1690   1800   1864     22    -23    133  A    N
ATOM   2767  CA  PRO A 588      13.861   2.313   9.194  1.00 13.50         A    C
ANISOU 2767  CA  PRO A 588     1699   1649   1781     24    -50     41  A    C
ATOM   2769  CB  PRO A 588      13.008   2.103  10.439  1.00 13.35         A    C
ANISOU 2769  CB  PRO A 588     1764   1590   1716     76    -62     -6  A    C
ATOM   2772  CG  PRO A 588      11.673   1.809   9.928  1.00 13.43         A    C
ANISOU 2772  CG  PRO A 588     1667   1761   1672    -40     50     68  A    C
ATOM   2775  CD  PRO A 588      11.504   2.628   8.662  1.00 13.91         A    C
ANISOU 2775  CD  PRO A 588     1743   1700   1839     16     29    104  A    C
ATOM   2778  C   PRO A 588      14.538   1.017   8.741  1.00 11.57         A    C
ANISOU 2778  C   PRO A 588     1422   1491   1483     21    -49      5  A    C
ATOM   2779  O   PRO A 588      14.303  -0.065   9.268  1.00 11.14         A    O
ANISOU 2779  O   PRO A 588     1294   1574   1361     81    -88     96  A    O
ATOM   2780  N   ILE A 589      15.387   1.146   7.738  1.00 10.87         A    N
ANISOU 2780  N   ILE A 589     1413   1343   1373     -5    -84     38  A    N
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ATOM   2782  CA  ILE A 589      15.941   0.000   7.051  1.00 10.49           A    C
ANISOU 2782  CA  ILE A 589    1291   1358   1337     16    -90     13  A    C
ATOM   2784  CB  ILE A 589      16.956   0.492   5.983  1.00 11.11           A    C
ANISOU 2784  CB  ILE A 589    1437   1403   1379    -34    -57     12  A    C
ATOM   2786  CG1 ILE A 589      16.248   1.248   4.851  1.00 12.77           A    C
ANISOU 2786  CG1 ILE A 589    1631   1555   1664     79    -43     70  A    C
ATOM   2789  CD1 ILE A 589      15.267   0.388   4.044  1.00 13.65           A    C
ANISOU 2789  CD1 ILE A 589    1905   1597   1681    -16    -40     94  A    C
ATOM   2793  CG2 ILE A 589      17.767  -0.643   5.436  1.00 10.86           A    C
ANISOU 2793  CG2 ILE A 589    1447   1421   1254    -71      5    -27  A    C
ATOM   2797  C   ILE A 589      16.622  -0.957   8.030  1.00 10.24           A    C
ANISOU 2797  C   ILE A 589    1371   1259   1262    -26    -33     49  A    C
ATOM   2798  O   ILE A 589      16.470  -2.163   7.911  1.00  9.58           A    O
ANISOU 2798  O   ILE A 589    1292   1125   1222     67   -143     57  A    O
ATOM   2799  N   LYS A 590      17.377  -0.415   8.987  1.00 10.07           A    N
ANISOU 2799  N   LYS A 590    1285   1253   1286     -3    -20     82  A    N
ATOM   2801  CA  LYS A 590      18.118  -1.241   9.958  1.00 10.34           A    C
ANISOU 2801  CA  LYS A 590    1334   1280   1312     33    -57     18  A    C
ATOM   2803  CB  LYS A 590      19.118  -0.367  10.716  1.00  9.88           A    C
ANISOU 2803  CB  LYS A 590    1334   1175   1244     26    -69    104  A    C
ATOM   2806  CG  LYS A 590      20.262   0.073   9.834  1.00 10.30           A    C
ANISOU 2806  CG  LYS A 590    1415   1305   1193     36      0     39  A    C
ATOM   2809  CD  LYS A 590      21.127   1.144  10.494  1.00 11.73           A    C
ANISOU 2809  CD  LYS A 590    1555   1358   1542    -46   -207    182  A    C
ATOM   2812  CE  LYS A 590      22.293   1.503   9.623  1.00 12.78           A    C
ANISOU 2812  CE  LYS A 590    1713   1558   1583    -12   -118     48  A    C
ATOM   2815  NZ  LYS A 590      23.216   2.545  10.173  1.00 14.55           A    N
ANISOU 2815  NZ  LYS A 590    1950   1654   1923    -89   -189    -17  A    N
ATOM   2819  C   LYS A 590      17.232  -2.059  10.923  1.00  9.74           A    C
ANISOU 2819  C   LYS A 590    1295   1165   1241     41    -59     24  A    C
ATOM   2820  O   LYS A 590      17.722  -2.929  11.657  1.00  9.82           A    O
ANISOU 2820  O   LYS A 590    1207   1237   1287     92   -113    118  A    O
ATOM   2821  N   TRP A 591      15.938  -1.740  10.960  1.00  9.17           A    N
ANISOU 2821  N   TRP A 591    1224   1156   1104     74     17     34  A    N
ATOM   2823  CA  TRP A 591      14.938  -2.432  11.754  1.00  9.07           A    C
ANISOU 2823  CA  TRP A 591    1188   1195   1061     10     10     20  A    C
ATOM   2825  CB  TRP A 591      14.051  -1.404  12.442  1.00 10.28           A    C
ANISOU 2825  CB  TRP A 591    1322   1298   1283     49    -32    -57  A    C
ATOM   2828  CG  TRP A 591      14.679  -0.623  13.537  1.00 10.96           A    C
ANISOU 2828  CG  TRP A 591    1478   1422   1263     66    -57    -46  A    C
ATOM   2829  CD1 TRP A 591      14.475  -0.795  14.883  1.00 12.24           A    C
ANISOU 2829  CD1 TRP A 591    1628   1561   1461    164     -9    -71  A    C
ATOM   2831  NE1 TRP A 591      15.162   0.164  15.582  1.00 13.31           A    N
ANISOU 2831  NE1 TRP A 591    1741   1547   1768    249    -62   -150  A    N
ATOM   2833  CE2 TRP A 591      15.841   0.977  14.719  1.00 12.60           A    C
ANISOU 2833  CE2 TRP A 591    1678   1550   1558    214    -99    -57  A    C
ATOM   2834  CD2 TRP A 591      15.525   0.538  13.408  1.00 10.95           A    C
ANISOU 2834  CD2 TRP A 591    1348   1395   1416    212    -69   -162  A    C
ATOM   2835  CE3 TRP A 591      16.075   1.228  12.328  1.00 13.22           A    C
ANISOU 2835  CE3 TRP A 591    1656   1554   1810     37    -31     14  A    C
ATOM   2837  CZ3 TRP A 591      16.897   2.342  12.567  1.00 14.15           A    C
ANISOU 2837  CZ3 TRP A 591    1859   1677   1837     89   -153    -55  A    C
ATOM   2839  CH2 TRP A 591      17.177   2.755  13.879  1.00 14.22           A    C
ANISOU 2839  CH2 TRP A 591    1867   1669   1866    134   -135   -110  A    C
ATOM   2841  CZ2 TRP A 591      16.659   2.090  14.962  1.00 13.23           A    C
ANISOU 2841  CZ2 TRP A 591    1675   1669   1681    211    -83    -98  A    C
ATOM   2843  C   TRP A 591      14.015  -3.349  10.940  1.00  9.10           A    C
ANISOU 2843  C   TRP A 591    1120   1220   1117    -80    106     27  A    C
ATOM   2844  O   TRP A 591      13.203  -4.078  11.509  1.00  9.60           A    O
ANISOU 2844  O   TRP A 591    1272   1285   1088   -186    226    128  A    O
ATOM   2845  N   MET A 592      14.123  -3.286   9.615  1.00  8.97           A    N
ANISOU 2845  N   MET A 592    1068   1302   1038    -63     34    -14  A    N
ATOM   2847  CA  MET A 592      13.138  -3.872   8.697  1.00  8.99           A    C
ANISOU 2847  CA  MET A 592    1065   1226   1124    -39    -14     28  A    C
ATOM   2849  CB  MET A 592      12.955  -2.949   7.475  1.00  9.42           A    C
ANISOU 2849  CB  MET A 592    1080   1294   1203    -52     26     62  A    C
ATOM   2852  CG  MET A 592      12.048  -1.807   7.767  1.00 11.87           A    C
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ANISOU 2852  CG  MET A 592     1370   1533   1605     31     -2     55  A    C
ATOM   2855  SD  MET A 592      12.167  -0.465   6.588  1.00 13.21           A    S
ANISOU 2855  SD  MET A 592     1673   1573   1773    144   -201     79  A    S
ATOM   2856  CE  MET A 592      11.778  -1.235   5.042  1.00 12.86           A    C
ANISOU 2856  CE  MET A 592     1482   1741   1663    -52    -90    106  A    C
ATOM   2860  C   MET A 592      13.463  -5.281   8.206  1.00  9.02           A    C
ANISOU 2860  C   MET A 592     1056   1225   1146    -35    -13      9  A    C
ATOM   2861  O   MET A 592      14.625  -5.652   8.029  1.00 10.06           A    O
ANISOU 2861  O   MET A 592     1321   1196   1304    119     13     -5  A    O
ATOM   2862  N   SER A 593      12.406  -6.058   7.968  1.00  9.29           A    N
ANISOU 2862  N   SER A 593     1059   1295   1173    -41    -22     40  A    N
ATOM   2864  CA  SER A 593      12.542  -7.395   7.428  1.00  9.43           A    C
ANISOU 2864  CA  SER A 593     1132   1284   1164    -23     -2     -1  A    C
ATOM   2866  CB  SER A 593      11.223  -8.158   7.405  1.00 10.04           A    C
ANISOU 2866  CB  SER A 593     1210   1360   1243    -15     18    -13  A    C
ATOM   2869  OG  SER A 593      10.389  -7.727   6.355  1.00 11.29           A    O
ANISOU 2869  OG  SER A 593     1284   1637   1367    -38     19      0  A    O
ATOM   2871  C   SER A 593      13.100  -7.345   6.017  1.00  9.22           A    C
ANISOU 2871  C   SER A 593     1105   1251   1146    -45     41     85  A    C
ATOM   2872  O   SER A 593      12.950  -6.322   5.324  1.00  9.98           A    O
ANISOU 2872  O   SER A 593     1353   1417   1019     10     35     73  A    O
ATOM   2873  N   PRO A 594      13.718  -8.436   5.576  1.00  8.91           A    N
ANISOU 2873  N   PRO A 594     1097   1209   1077    -50     71     65  A    N
ATOM   2874  CA  PRO A 594      14.227  -8.463   4.188  1.00  9.59           A    C
ANISOU 2874  CA  PRO A 594     1197   1262   1185    -47     55     19  A    C
ATOM   2876  CB  PRO A 594      14.833  -9.853   4.045  1.00 10.47           A    C
ANISOU 2876  CB  PRO A 594     1271   1343   1360    -20     73     48  A    C
ATOM   2879  CG  PRO A 594      15.100 -10.293   5.442  1.00 11.63           A    C
ANISOU 2879  CG  PRO A 594     1509   1514   1393     13     31      2  A    C
ATOM   2882  CD  PRO A 594      14.062  -9.666   6.321  1.00 10.26           A    C
ANISOU 2882  CD  PRO A 594     1211   1294   1390    -94      8     -6  A    C
ATOM   2885  C   PRO A 594      13.157  -8.210   3.160  1.00  9.30           A    C
ANISOU 2885  C   PRO A 594     1180   1239   1112    -36     74    -34  A    C
ATOM   2886  O   PRO A 594      13.400  -7.501   2.210  1.00 10.37           A    O
ANISOU 2886  O   PRO A 594     1249   1378   1312     18    -47    150  A    O
ATOM   2887  N   GLU A 595      11.976  -8.763   3.347  1.00 10.12           A    N
ANISOU 2887  N   GLU A 595     1297   1385   1163    -32    -11     27  A    N
ATOM   2889  CA  GLU A 595      10.911  -8.579   2.375  1.00 10.05           A    C
ANISOU 2889  CA  GLU A 595     1222   1302   1292    -13    -47      0  A    C
ATOM   2891  CB  GLU A 595       9.809  -9.610   2.584  1.00 10.60           A    C
ANISOU 2891  CB  GLU A 595     1315   1411   1298    -52     -7     42  A    C
ATOM   2894  CG  GLU A 595       8.953  -9.471   3.827  1.00 11.26           A    C
ANISOU 2894  CG  GLU A 595     1336   1498   1442   -130      5     -6  A    C
ATOM   2897  CD  GLU A 595       9.485 -10.178   5.054  1.00 11.56           A    C
ANISOU 2897  CD  GLU A 595     1394   1580   1418     28     28     35  A    C
ATOM   2898  OE1 GLU A 595      10.685 -10.577   5.091  1.00 11.13           A    O
ANISOU 2898  OE1 GLU A 595     1434   1517   1277    -69     73     78  A    O
ATOM   2899  OE2 GLU A 595       8.670 -10.321   6.019  1.00 11.62           A    O
ANISOU 2899  OE2 GLU A 595     1484   1457   1472     42    121     -5  A    O
ATOM   2900  C   GLU A 595      10.383  -7.144   2.371  1.00  9.21           A    C
ANISOU 2900  C   GLU A 595     1136   1262   1100     37     30      8  A    C
ATOM   2901  O   GLU A 595       9.883  -6.656   1.347  1.00  9.76           A    O
ANISOU 2901  O   GLU A 595     1097   1442   1167     -2    -68    -41  A    O
ATOM   2902  N   SER A 596      10.500  -6.452   3.501  1.00  9.67           A    N
ANISOU 2902  N   SER A 596     1235   1236   1203     -7    -38     28  A    N
ATOM   2904  CA  SER A 596      10.129  -5.052   3.558  1.00  9.89           A    C
ANISOU 2904  CA  SER A 596     1196   1260   1299    -21    -28     25  A    C
ATOM   2906  CB  SER A 596      10.008  -4.594   5.008  1.00 10.23           A    C
ANISOU 2906  CB  SER A 596     1287   1329   1268    -75    105     98  A    C
ATOM   2909  OG  SER A 596       9.052  -5.376   5.764  1.00 10.32           A    O
ANISOU 2909  OG  SER A 596     1213   1403   1302   -145    245    197  A    O
ATOM   2911  C   SER A 596      11.171  -4.200   2.827  1.00  9.96           A    C
ANISOU 2911  C   SER A 596     1248   1278   1255    -10    -22     46  A    C
ATOM   2912  O   SER A 596      10.830  -3.244   2.133  1.00  9.77           A    O
ANISOU 2912  O   SER A 596     1240   1189   1281    -62    -68     33  A    O
ATOM   2913  N   ILE A 597      12.441  -4.557   2.970  1.00 10.01           A    N
ANISOU 2913  N   ILE A 597     1255   1266   1280    -33    -36     89  A    N
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ATOM   2915  CA  ILE A 597      13.514  -3.836   2.286  1.00  9.56           A    C
ANISOU 2915  CA  ILE A 597    1210   1283   1136    -35     10       0  A    C
ATOM   2917  CB  ILE A 597      14.901  -4.252   2.834  1.00  9.88           A    C
ANISOU 2917  CB  ILE A 597    1284   1340   1130    -70    -42      60  A    C
ATOM   2919  CG1 ILE A 597      15.037  -3.816   4.304  1.00  9.44           A    C
ANISOU 2919  CG1 ILE A 597    1175   1212   1197      2     76     -30  A    C
ATOM   2922  CD1 ILE A 597      16.240  -4.356   4.994  1.00 10.48           A    C
ANISOU 2922  CD1 ILE A 597    1424   1480   1077     41    -61     -30  A    C
ATOM   2926  CG2 ILE A 597      16.019  -3.627   1.970  1.00 10.27           A    C
ANISOU 2926  CG2 ILE A 597    1248   1426   1228    -93    -42      58  A    C
ATOM   2930  C   ILE A 597      13.438  -4.070   0.778  1.00  9.98           A    C
ANISOU 2930  C   ILE A 597    1320   1345   1126    -41      7      69  A    C
ATOM   2931  O   ILE A 597      13.494  -3.129  -0.030  1.00 10.68           A    O
ANISOU 2931  O   ILE A 597    1422   1278   1357    -44    -20     162  A    O
ATOM   2932  N   ASN A 598      13.296  -5.320   0.405  1.00 10.21           A    N
ANISOU 2932  N   ASN A 598    1380   1360   1138    -50     35      30  A    N
ATOM   2934  CA  ASN A 598      13.343  -5.707  -1.024  1.00 10.75           A    C
ANISOU 2934  CA  ASN A 598    1425   1458   1199    -28      8      11  A    C
ATOM   2936  CB  ASN A 598      13.584  -7.212  -1.153  1.00 10.68           A    C
ANISOU 2936  CB  ASN A 598    1402   1431   1225    -25     49     -13  A    C
ATOM   2939  CG  ASN A 598      15.020  -7.605  -0.903  1.00 12.94           A    C
ANISOU 2939  CG  ASN A 598    1649   1748   1519    -65   -177      39  A    C
ATOM   2940  OD1 ASN A 598      15.945  -6.851  -1.204  1.00 14.53           A    O
ANISOU 2940  OD1 ASN A 598    1544   2190   1787    -17     89     -14  A    O
ATOM   2941  ND2 ASN A 598      15.217  -8.832  -0.397  1.00 14.73           A    N
ANISOU 2941  ND2 ASN A 598    2011   1799   1785    -55   -246      29  A    N
ATOM   2944  C   ASN A 598      12.079  -5.365  -1.807  1.00 11.61           A    C
ANISOU 2944  C   ASN A 598    1470   1606   1334    -17     23      58  A    C
ATOM   2945  O   ASN A 598      12.150  -4.927  -2.954  1.00 11.95           A    O
ANISOU 2945  O   ASN A 598    1598   1738   1203    -74     48      74  A    O
ATOM   2946  N   PHE A 599      10.915  -5.571  -1.192  1.00 11.13           A    N
ANISOU 2946  N   PHE A 599    1371   1614   1244    -82    -19      43  A    N
ATOM   2948  CA  PHE A 599       9.643  -5.530  -1.925  1.00 11.86           A    C
ANISOU 2948  CA  PHE A 599    1459   1606   1441     -1    -54      39  A    C
ATOM   2950  CB  PHE A 599       9.109  -6.949  -2.112  1.00 12.27           A    C
ANISOU 2950  CB  PHE A 599    1511   1667   1480     -4    -80     -27  A    C
ATOM   2953  CG  PHE A 599      10.116  -7.904  -2.688  1.00 13.95           A    C
ANISOU 2953  CG  PHE A 599    1691   1826   1781      0    -47     -36  A    C
ATOM   2954  CD1 PHE A 599      10.758  -7.627  -3.890  1.00 14.56           A    C
ANISOU 2954  CD1 PHE A 599    1774   1899   1856     34      7     -17  A    C
ATOM   2956  CE1 PHE A 599      11.700  -8.503  -4.401  1.00 16.51           A    C
ANISOU 2956  CE1 PHE A 599    2048   2000   2223     24     41     -25  A    C
ATOM   2958  CZ  PHE A 599      11.999  -9.653  -3.717  1.00 15.93           A    C
ANISOU 2958  CZ  PHE A 599    1918   2030   2105    101     41     -31  A    C
ATOM   2960  CE2 PHE A 599      11.372  -9.948  -2.549  1.00 16.28           A    C
ANISOU 2960  CE2 PHE A 599    1991   2025   2166      1    -15     -19  A    C
ATOM   2962  CD2 PHE A 599      10.447  -9.066  -2.013  1.00 14.63           A    C
ANISOU 2962  CD2 PHE A 599    1831   1797   1928    -41      5     -23  A    C
ATOM   2964  C   PHE A 599       8.584  -4.682  -1.247  1.00 11.77           A    C
ANISOU 2964  C   PHE A 599    1463   1608   1400    -24    -39      33  A    C
ATOM   2965  O   PHE A 599       7.439  -4.693  -1.660  1.00 12.18           A    O
ANISOU 2965  O   PHE A 599    1468   1661   1496   -153   -124      52  A    O
ATOM   2966  N   ARG A 600       8.969  -3.947  -0.204  1.00 11.50           A    N
ANISOU 2966  N   ARG A 600    1459   1527   1382     18    -42      -6  A    N
ATOM   2968  CA  ARG A 600       8.033  -3.173   0.604  1.00 11.53           A    C
ANISOU 2968  CA  ARG A 600    1463   1514   1401     22    -24      24  A    C
ATOM   2970  CB  ARG A 600       7.636  -1.887  -0.143  1.00 11.85           A    C
ANISOU 2970  CB  ARG A 600    1556   1479   1467    -23     37      48  A    C
ATOM   2973  CG  ARG A 600       8.808  -0.969  -0.430  1.00 11.41           A    C
ANISOU 2973  CG  ARG A 600    1458   1483   1393     42    -17      84  A    C
ATOM   2976  CD  ARG A 600       9.327  -0.272   0.803  1.00 13.18           A    C
ANISOU 2976  CD  ARG A 600    1633   1644   1730     22    -38     -12  A    C
ATOM   2979  NE  ARG A 600      10.395   0.643   0.428  1.00 14.17           A    N
ANISOU 2979  NE  ARG A 600    1837   1614   1929     10     -3     133  A    N
ATOM   2981  CZ  ARG A 600      11.695   0.379   0.489  1.00 15.98           A    C
ANISOU 2981  CZ  ARG A 600    1894   1988   2189     25     -3      14  A    C
ATOM   2982  NH1 ARG A 600      12.141  -0.779   0.959  1.00 15.36           A    N
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ANISOU 2982  NH1 ARG A 600     1832   1945   2057   -104    -33    126  A    N
ATOM   2985  NH2 ARG A 600      12.561   1.294   0.074  1.00 17.80        A    N
ANISOU 2985  NH2 ARG A 600     2293   2177   2291    -95      1     95  A    N
ATOM   2988  C   ARG A 600      6.813  -3.997   0.991  1.00 12.03        A    C
ANISOU 2988  C   ARG A 600     1525   1555   1488      4     21     66  A    C
ATOM   2989  O   ARG A 600      5.667  -3.540   0.899  1.00 12.71        A    O
ANISOU 2989  O   ARG A 600     1640   1649   1538     89     68    216  A    O
ATOM   2990  N   ARG A 601      7.089  -5.218   1.452  1.00 11.58        A    N
ANISOU 2990  N   ARG A 601     1417   1563   1419      7    -49     58  A    N
ATOM   2992  CA  ARG A 601      6.078  -6.128   1.965  1.00 11.44        A    C
ANISOU 2992  CA  ARG A 601     1424   1551   1369    -12    -37     53  A    C
ATOM   2994  CB  ARG A 601      6.463  -7.563   1.637  1.00 12.67        A    C
ANISOU 2994  CB  ARG A 601     1588   1663   1561    -10    -91    -57  A    C
ATOM   2997  CG  ARG A 601      5.472  -8.612   2.069  1.00 14.91        A    C
ANISOU 2997  CG  ARG A 601     1851   1995   1818    -34    -14     61  A    C
ATOM   3000  CD  ARG A 601      5.697  -9.952   1.382  1.00 17.74        A    C
ANISOU 3000  CD  ARG A 601     2258   2106   2374      4      7     -3  A    C
ATOM   3003  NE  ARG A 601      5.514  -9.784  -0.057  1.00 19.66        A    N
ANISOU 3003  NE  ARG A 601     2617   2382   2468     87    -41    -10  A    N
ATOM   3005  CZ  ARG A 601      6.285 -10.267  -1.029  1.00 21.00        A    C
ANISOU 3005  CZ  ARG A 601     2561   2753   2663    -11     86     53  A    C
ATOM   3006  NH1 ARG A 601      7.357 -11.018  -0.784  1.00 22.47        A    N
ANISOU 3006  NH1 ARG A 601     2809   2782   2946     79     -1    100  A    N
ATOM   3009  NH2 ARG A 601      5.983  -9.979  -2.280  1.00 19.82        A    N
ANISOU 3009  NH2 ARG A 601     2298   2580   2652     95    -57     78  A    N
ATOM   3012  C   ARG A 601      6.063  -5.963   3.470  1.00 11.15        A    C
ANISOU 3012  C   ARG A 601     1403   1500   1332    -36    -18     53  A    C
ATOM   3013  O   ARG A 601      7.066  -6.212   4.126  1.00 11.96        A    O
ANISOU 3013  O   ARG A 601     1567   1654   1321     43     73     60  A    O
ATOM   3014  N   PHE A 602      4.931  -5.518   3.991  1.00 10.72        A    N
ANISOU 3014  N   PHE A 602     1378   1494   1199     36     21     77  A    N
ATOM   3016  CA  PHE A 602      4.763  -5.308   5.412  1.00 10.99        A    C
ANISOU 3016  CA  PHE A 602     1305   1548   1321    -15     23     61  A    C
ATOM   3018  CB  PHE A 602      4.545  -3.851   5.713  1.00 11.03        A    C
ANISOU 3018  CB  PHE A 602     1315   1509   1364     -7     22     36  A    C
ATOM   3021  CG  PHE A 602      5.689  -2.951   5.331  1.00 11.43        A    C
ANISOU 3021  CG  PHE A 602     1386   1493   1461      0     52     74  A    C
ATOM   3022  CD1 PHE A 602      6.668  -2.610   6.273  1.00 13.11        A    C
ANISOU 3022  CD1 PHE A 602     1529   1757   1691     -1    -61    185  A    C
ATOM   3024  CE1 PHE A 602      7.746  -1.771   5.922  1.00 13.50        A    C
ANISOU 3024  CE1 PHE A 602     1500   1892   1736     21     45    -12  A    C
ATOM   3026  CZ  PHE A 602      7.788  -1.239   4.645  1.00 14.36        A    C
ANISOU 3026  CZ  PHE A 602     1731   1858   1865     51     24     94  A    C
ATOM   3028  CE2 PHE A 602      6.813  -1.558   3.712  1.00 13.34        A    C
ANISOU 3028  CE2 PHE A 602     1681   1625   1762     52    114    -48  A    C
ATOM   3030  CD2 PHE A 602      5.775  -2.418   4.052  1.00 14.19        A    C
ANISOU 3030  CD2 PHE A 602     1724   1964   1702    -10     36     88  A    C
ATOM   3032  C   PHE A 602      3.551  -6.087   5.905  1.00 10.54        A    C
ANISOU 3032  C   PHE A 602     1148   1469   1386    -13     -1    116  A    C
ATOM   3033  O   PHE A 602      2.407  -5.842   5.488  1.00 12.65        A    O
ANISOU 3033  O   PHE A 602     1365   1889   1551    108    -29    211  A    O
ATOM   3034  N   THR A 603      3.811  -7.023   6.796  1.00 11.08        A    N
ANISOU 3034  N   THR A 603     1222   1582   1405    -24      4    106  A    N
ATOM   3036  CA  THR A 603      2.816  -7.938   7.319  1.00 11.28        A    C
ANISOU 3036  CA  THR A 603     1328   1523   1433    -28    -70     66  A    C
ATOM   3038  CB  THR A 603      2.983  -9.312   6.670  1.00 12.02        A    C
ANISOU 3038  CB  THR A 603     1395   1663   1507     -1     31    -12  A    C
ATOM   3040  OG1 THR A 603      4.240  -9.900   7.083  1.00 13.58        A    O
ANISOU 3040  OG1 THR A 603     1799   1882   1478    121    -99     64  A    O
ATOM   3042  CG2 THR A 603      2.992  -9.233   5.109  1.00 13.80        A    C
ANISOU 3042  CG2 THR A 603     1655   1915   1669    -17    -57      7  A    C
ATOM   3046  C   THR A 603      3.050  -8.096   8.812  1.00 10.70        A    C
ANISOU 3046  C   THR A 603     1306   1392   1365     -8    -32     68  A    C
ATOM   3047  O   THR A 603      3.999  -7.564   9.368  1.00 10.54        A    O
ANISOU 3047  O   THR A 603     1282   1352   1369     -5     25    -23  A    O
ATOM   3048  N   THR A 604      2.189  -8.848   9.478  1.00 10.68        A    N
ANISOU 3048  N   THR A 604     1218   1508   1329    -17     23     81  A    N
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ATOM   3050  CA  THR A 604       2.465  -9.157  10.874  1.00 10.95           A    C
ANISOU 3050  CA  THR A 604    1327   1474   1358    -15     13     41  A    C
ATOM   3052  CB  THR A 604       1.306  -9.959  11.474  1.00 12.36           A    C
ANISOU 3052  CB  THR A 604    1400   1764   1533     21     54    140  A    C
ATOM   3054  OG1 THR A 604       0.140  -9.113  11.538  1.00 15.22           A    O
ANISOU 3054  OG1 THR A 604    1720   2173   1887    218     80    -10  A    O
ATOM   3056  CG2 THR A 604       1.597 -10.335  12.915  1.00 14.21           A    C
ANISOU 3056  CG2 THR A 604    1763   1889   1746     -3     32     55  A    C
ATOM   3060  C   THR A 604       3.814  -9.877  11.035  1.00 10.39           A    C
ANISOU 3060  C   THR A 604    1301   1384   1260    -57     34     32  A    C
ATOM   3061  O   THR A 604       4.513  -9.634  12.009  1.00 10.09           A    O
ANISOU 3061  O   THR A 604    1291   1435   1106    -33     61    -16  A    O
ATOM   3062  N   ALA A 605       4.208 -10.710  10.062  1.00  9.88           A    N
ANISOU 3062  N   ALA A 605    1244   1284   1226    -46     -3     22  A    N
ATOM   3064  CA  ALA A 605       5.500 -11.361  10.095  1.00  9.56           A    C
ANISOU 3064  CA  ALA A 605    1219   1168   1244    -45     46     14  A    C
ATOM   3066  CB  ALA A 605       5.625 -12.414   9.019  1.00  9.71           A    C
ANISOU 3066  CB  ALA A 605    1094   1242   1353    -73      5    -81  A    C
ATOM   3070  C   ALA A 605       6.675 -10.385   9.998  1.00  9.33           A    C
ANISOU 3070  C   ALA A 605    1124   1231   1190    -37    -11     -7  A    C
ATOM   3071  O   ALA A 605       7.711 -10.608  10.637  1.00  8.88           A    O
ANISOU 3071  O   ALA A 605    1140   1174   1059     41    -46     60  A    O
ATOM   3072  N   SER A 606       6.512  -9.307   9.241  1.00  8.76           A    N
ANISOU 3072  N   SER A 606    1154   1124   1049    -29     11    -27  A    N
ATOM   3074  CA  SER A 606       7.539  -8.278   9.219  1.00  8.84           A    C
ANISOU 3074  CA  SER A 606    1100   1210   1046    -25     -9     32  A    C
ATOM   3076  CB  SER A 606       7.487  -7.363   7.991  1.00  9.46           A    C
ANISOU 3076  CB  SER A 606    1308   1122   1160    -61     73     61  A    C
ATOM   3079  OG  SER A 606       6.365  -6.519   7.970  1.00 12.44           A    O
ANISOU 3079  OG  SER A 606    1548   1453   1726     70     55    153  A    O
ATOM   3081  C   SER A 606       7.590  -7.503  10.539  1.00  8.37           A    C
ANISOU 3081  C   SER A 606    1078   1081   1020     -8     -5     24  A    C
ATOM   3082  O   SER A 606       8.670  -7.107  10.981  1.00  9.31           A    O
ANISOU 3082  O   SER A 606    1114   1306   1116    -30    -37    167  A    O
ATOM   3083  N   ASP A 607       6.433  -7.317  11.174  1.00  8.77           A    N
ANISOU 3083  N   ASP A 607    1027   1217   1086    -30      8     47  A    N
ATOM   3085  CA  ASP A 607       6.384  -6.745  12.523  1.00  8.49           A    C
ANISOU 3085  CA  ASP A 607    1053   1109   1061    -60     50     41  A    C
ATOM   3087  CB  ASP A 607       4.954  -6.516  13.002  1.00  8.95           A    C
ANISOU 3087  CB  ASP A 607    1100   1190   1108     30    -32     -3  A    C
ATOM   3090  CG  ASP A 607       4.360  -5.209  12.593  1.00 10.83           A    C
ANISOU 3090  CG  ASP A 607    1321   1330   1461     26    120      7  A    C
ATOM   3091  OD1 ASP A 607       5.011  -4.305  11.994  1.00 13.04           A    O
ANISOU 3091  OD1 ASP A 607    1672   1415   1865     89    -72     76  A    O
ATOM   3092  OD2 ASP A 607       3.139  -5.054  12.856  1.00 13.25           A    O
ANISOU 3092  OD2 ASP A 607    1351   1773   1908    156    134    269  A    O
ATOM   3093  C   ASP A 607       7.111  -7.650  13.546  1.00  8.81           A    C
ANISOU 3093  C   ASP A 607    1106   1106   1136    -29      4     21  A    C
ATOM   3094  O   ASP A 607       7.754  -7.143  14.458  1.00  8.69           A    O
ANISOU 3094  O   ASP A 607    1188    931   1183     33    -77     88  A    O
ATOM   3095  N   VAL A 608       7.008  -8.969  13.395  1.00  8.75           A    N
ANISOU 3095  N   VAL A 608    1030   1131   1163     11    -21     72  A    N
ATOM   3097  CA  VAL A 608       7.718  -9.894  14.282  1.00  8.19           A    C
ANISOU 3097  CA  VAL A 608     873   1051   1188     76     60     39  A    C
ATOM   3099  CB  VAL A 608       7.320 -11.353  14.019  1.00  8.71           A    C
ANISOU 3099  CB  VAL A 608     907   1144   1256    -42     39     19  A    C
ATOM   3101  CG1 VAL A 608       8.255 -12.340  14.695  1.00  8.72           A    C
ANISOU 3101  CG1 VAL A 608     822   1138   1350    -60     25      5  A    C
ATOM   3105  CG2 VAL A 608       5.884 -11.612  14.519  1.00  9.27           A    C
ANISOU 3105  CG2 VAL A 608    1017   1114   1389    -43     45      2  A    C
ATOM   3109  C   VAL A 608       9.237  -9.701  14.158  1.00  8.48           A    C
ANISOU 3109  C   VAL A 608     994   1166   1060     -4     45     33  A    C
ATOM   3110  O   VAL A 608       9.932  -9.625  15.166  1.00  8.08           A    O
ANISOU 3110  O   VAL A 608     889   1062   1118     70     11     48  A    O
ATOM   3111  N   TRP A 609       9.729  -9.606  12.914  1.00  8.33           A    N
ANISOU 3111  N   TRP A 609    1007   1249    908    -41     26     37  A    N
ATOM   3113  CA  TRP A 609      11.142  -9.320  12.681  1.00  8.34           A    C
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ANISOU 3113  CA  TRP A 609     1059   1133    977     22     17     21  A    C
ATOM   3115  CB  TRP A 609      11.385  -9.180  11.178  1.00  7.90       A    C
ANISOU 3115  CB  TRP A 609     1066   1075    858    -48     94   -113  A    C
ATOM   3118  CG  TRP A 609      12.771  -8.768  10.842  1.00  7.50       A    C
ANISOU 3118  CG  TRP A 609      971    909    969    -33     17     -5  A    C
ATOM   3119  CD1 TRP A 609      13.368  -7.539  11.112  1.00  8.81       A    C
ANISOU 3119  CD1 TRP A 609     1188   1085   1072     38      1   -215  A    C
ATOM   3121  NE1 TRP A 609      14.670  -7.550  10.672  1.00  9.39       A    N
ANISOU 3121  NE1 TRP A 609     1136   1203   1229    -39     41   -112  A    N
ATOM   3123  CE2 TRP A 609      14.948  -8.779  10.124  1.00  8.49       A    C
ANISOU 3123  CE2 TRP A 609     1078   1034   1111    -54    -43    -58  A    C
ATOM   3124  CD2 TRP A 609      13.778  -9.573  10.215  1.00  8.13       A    C
ANISOU 3124  CD2 TRP A 609     1005   1075   1008    -51     39     41  A    C
ATOM   3125  CE3 TRP A 609      13.805 -10.880   9.692  1.00  9.35       A    C
ANISOU 3125  CE3 TRP A 609     1122   1339   1091    -34    -66     -2  A    C
ATOM   3127  CZ3 TRP A 609      14.975 -11.352   9.124  1.00  9.86       A    C
ANISOU 3127  CZ3 TRP A 609     1363   1168   1214     18     39    -41  A    C
ATOM   3129  CH2 TRP A 609      16.119 -10.542   9.073  1.00 10.57       A    C
ANISOU 3129  CH2 TRP A 609     1332   1373   1311    -13     31     38  A    C
ATOM   3131  CZ2 TRP A 609      16.118  -9.251   9.555  1.00  9.41       A    C
ANISOU 3131  CZ2 TRP A 609     1017   1411   1144      7    -67     18  A    C
ATOM   3133  C   TRP A 609      11.524  -8.025  13.419  1.00  8.26       A    C
ANISOU 3133  C   TRP A 609     1006   1063   1067    -28     48     58  A    C
ATOM   3134  O   TRP A 609      12.522  -7.955  14.143  1.00  8.86       A    O
ANISOU 3134  O   TRP A 609     1113   1169   1082     -1     -5     40  A    O
ATOM   3135  N   MET A 610      10.728  -6.980  13.217  1.00  8.69       A    N
ANISOU 3135  N   MET A 610     1029   1163   1106      0     56     35  A    N
ATOM   3137  CA  MET A 610      11.045  -5.673  13.757  1.00  8.50       A    C
ANISOU 3137  CA  MET A 610     1051   1120   1058      1     22     39  A    C
ATOM   3139  CB  MET A 610      10.134  -4.623  13.150  1.00  9.27       A    C
ANISOU 3139  CB  MET A 610     1139   1280   1101     60     34    -12  A    C
ATOM   3142  CG  MET A 610      10.465  -3.184  13.554  1.00 10.66       A    C
ANISOU 3142  CG  MET A 610     1372   1304   1374     75     19    122  A    C
ATOM   3145  SD  MET A 610       9.370  -1.993  12.813  1.00 11.18       A    S
ANISOU 3145  SD  MET A 610     1461   1256   1529    218    165    197  A    S
ATOM   3146  CE  MET A 610      10.494  -0.555  12.750  1.00 13.95       A    C
ANISOU 3146  CE  MET A 610     1693   1720   1888     12    180    244  A    C
ATOM   3150  C   MET A 610      10.990  -5.686  15.277  1.00  7.98       A    C
ANISOU 3150  C   MET A 610     964   1022   1045     27      8     93  A    C
ATOM   3151  O   MET A 610      11.813  -5.085  15.942  1.00  8.54       A    O
ANISOU 3151  O   MET A 610     1078   1087   1077    -42     -4     80  A    O
ATOM   3152  N   PHE A 611      10.020  -6.403  15.820  1.00  7.88       A    N
ANISOU 3152  N   PHE A 611     971    966   1056     -6     14     51  A    N
ATOM   3154  CA  PHE A 611       9.902  -6.526  17.253  1.00  7.74       A    C
ANISOU 3154  CA  PHE A 611     954    964   1021     33     53     60  A    C
ATOM   3156  CB  PHE A 611       8.656  -7.320  17.632  1.00  8.72       A    C
ANISOU 3156  CB  PHE A 611     1082   1057   1173     50    108     24  A    C
ATOM   3159  CG  PHE A 611       8.637  -7.708  19.069  1.00  8.66       A    C
ANISOU 3159  CG  PHE A 611     1036   1145   1107     62   -101    -66  A    C
ATOM   3160  CD1 PHE A 611       8.388  -6.763  20.065  1.00  9.74       A    C
ANISOU 3160  CD1 PHE A 611     1260   1295   1144     25     69    -16  A    C
ATOM   3162  CE1 PHE A 611       8.405  -7.126  21.393  1.00  9.58       A    C
ANISOU 3162  CE1 PHE A 611     1340   1276   1022    171    112   -179  A    C
ATOM   3164  CZ  PHE A 611       8.663  -8.428  21.753  1.00  9.63       A    C
ANISOU 3164  CZ  PHE A 611     1105   1320   1231     -6     47    118  A    C
ATOM   3166  CE2 PHE A 611       8.879  -9.378  20.784  1.00 10.44       A    C
ANISOU 3166  CE2 PHE A 611     1387   1241   1339     13    -95    120  A    C
ATOM   3168  CD2 PHE A 611       8.872  -9.022  19.432  1.00  9.85       A    C
ANISOU 3168  CD2 PHE A 611     1285   1223   1233    107     12      3  A    C
ATOM   3170  C   PHE A 611      11.153  -7.145  17.870  1.00  7.02       A    C
ANISOU 3170  C   PHE A 611     904    921    840     31    110     22  A    C
ATOM   3171  O   PHE A 611      11.620  -6.710  18.933  1.00  8.57       A    O
ANISOU 3171  O   PHE A 611     996   1108   1152    113      3     51  A    O
ATOM   3172  N   ALA A 612      11.722  -8.144  17.199  1.00  7.13       A    N
ANISOU 3172  N   ALA A 612     1009    847    851     65     20      6  A    N
ATOM   3174  CA  ALA A 612      12.970  -8.721  17.694  1.00  7.74       A    C
ANISOU 3174  CA  ALA A 612     990   1002    947     24     11     28  A    C
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ATOM   3176  CB  ALA A 612      13.295 -10.000  17.023  1.00  8.53           A    C
ANISOU 3176  CB  ALA A 612    1135    993   1113     22     51    103  A    C
ATOM   3180  C   ALA A 612      14.125  -7.733  17.628  1.00  7.90           A    C
ANISOU 3180  C   ALA A 612    1004    940   1056     95     26    -10  A    C
ATOM   3181  O   ALA A 612      15.001  -7.758  18.493  1.00  8.27           A    O
ANISOU 3181  O   ALA A 612    1085   1012   1044    -55     21     68  A    O
ATOM   3182  N   VAL A 613      14.148  -6.862  16.615  1.00  7.47           A    N
ANISOU 3182  N   VAL A 613     887   1023    925     54     34      1  A    N
ATOM   3184  CA  VAL A 613      15.130  -5.771  16.598  1.00  7.74           A    C
ANISOU 3184  CA  VAL A 613     916   1032    990     29     25    -11  A    C
ATOM   3186  CB  VAL A 613      15.124  -4.954  15.294  1.00  8.08           A    C
ANISOU 3186  CB  VAL A 613     979   1066   1025    -31     61    -16  A    C
ATOM   3188  CG1 VAL A 613      16.212  -3.903  15.326  1.00  8.94           A    C
ANISOU 3188  CG1 VAL A 613    1125   1147   1125    -76     26     41  A    C
ATOM   3192  CG2 VAL A 613      15.295  -5.871  14.104  1.00  7.92           A    C
ANISOU 3192  CG2 VAL A 613     974    918   1114     56    -26     54  A    C
ATOM   3196  C   VAL A 613      14.924  -4.850  17.811  1.00  7.57           A    C
ANISOU 3196  C   VAL A 613     913   1072    891    -49      4     17  A    C
ATOM   3197  O   VAL A 613      15.867  -4.477  18.469  1.00  8.37           A    O
ANISOU 3197  O   VAL A 613     960   1207   1013   -104    -33     18  A    O
ATOM   3198  N   CYS A 614      13.677  -4.522  18.103  1.00  8.43           A    N
ANISOU 3198  N   CYS A 614    1052   1065   1085     16    -28    -41  A    N
ATOM   3200  CA  CYS A 614      13.374  -3.718  19.264  1.00  8.40           A    C
ANISOU 3200  CA  CYS A 614    1021   1112   1056     36     58    -15  A    C
ATOM   3202  CB  CYS A 614      11.865  -3.464  19.290  1.00  9.06           A    C
ANISOU 3202  CB  CYS A 614    1089   1165   1187     64     61     30  A    C
ATOM   3205  SG  CYS A 614      11.324  -2.366  20.621  1.00 11.65           A    S
ANISOU 3205  SG  CYS A 614    1381   1541   1503    381    -28   -304  A    S
ATOM   3206  C   CYS A 614      13.867  -4.397  20.564  1.00  8.29           A    C
ANISOU 3206  C   CYS A 614    1023   1002   1125    -25     30    -23  A    C
ATOM   3207  O   CYS A 614      14.461  -3.744  21.429  1.00  9.16           A    O
ANISOU 3207  O   CYS A 614    1032   1308   1138     27     -9     -4  A    O
ATOM   3208  N   MET A 615      13.654  -5.708  20.688  1.00  8.27           A    N
ANISOU 3208  N   MET A 615     994    985   1163    -60      3     92  A    N
ATOM   3210  CA  MET A 615      14.185  -6.416  21.852  1.00  8.60           A    C
ANISOU 3210  CA  MET A 615    1117   1096   1054     24     48     18  A    C
ATOM   3212  CB  MET A 615      13.794  -7.892  21.841  1.00  9.35           A    C
ANISOU 3212  CB  MET A 615    1195   1150   1207    -33     -6      0  A    C
ATOM   3215  CG  MET A 615      12.336  -8.165  22.031  1.00 10.66           A    C
ANISOU 3215  CG  MET A 615    1304   1337   1409      0     67    118  A    C
ATOM   3218  SD  MET A 615      11.989  -9.904  22.526  1.00 13.11           A    S
ANISOU 3218  SD  MET A 615    1496   1477   2007   -159     83    378  A    S
ATOM   3219  CE  MET A 615      12.205 -10.770  20.949  1.00 14.46           A    C
ANISOU 3219  CE  MET A 615    1773   1582   2138    -87    155     76  A    C
ATOM   3223  C   MET A 615      15.691  -6.323  21.906  1.00  8.07           A    C
ANISOU 3223  C   MET A 615    1079    956   1029     55     23     41  A    C
ATOM   3224  O   MET A 615      16.261  -6.134  22.977  1.00  8.96           A    O
ANISOU 3224  O   MET A 615    1292   1100   1012    121     83     13  A    O
ATOM   3225  N   TRP A 616      16.349  -6.428  20.748  1.00  8.09           A    N
ANISOU 3225  N   TRP A 616    1112   1019    939    114    -49     27  A    N
ATOM   3227  CA  TRP A 616      17.802  -6.264  20.692  1.00  8.17           A    C
ANISOU 3227  CA  TRP A 616    1131   1004    966     75    -26     -3  A    C
ATOM   3229  CB  TRP A 616      18.327  -6.540  19.276  1.00  8.03           A    C
ANISOU 3229  CB  TRP A 616    1125    939    985     85     20     19  A    C
ATOM   3232  CG  TRP A 616      19.790  -6.449  19.151  1.00  7.37           A    C
ANISOU 3232  CG  TRP A 616    1017    909    873     22    -84    -42  A    C
ATOM   3233  CD1 TRP A 616      20.648  -7.482  19.193  1.00  8.05           A    C
ANISOU 3233  CD1 TRP A 616    1119   1061    877    129     70     68  A    C
ATOM   3235  NE1 TRP A 616      21.940  -7.044  19.044  1.00  8.55           A    N
ANISOU 3235  NE1 TRP A 616    1074   1128   1046     63     24     22  A    N
ATOM   3237  CE2 TRP A 616      21.946  -5.686  18.895  1.00  8.19           A    C
ANISOU 3237  CE2 TRP A 616    1105   1016    988      9    -27      3  A    C
ATOM   3238  CD2 TRP A 616      20.592  -5.268  18.938  1.00  8.11           A    C
ANISOU 3238  CD2 TRP A 616    1033    993   1056     27     43     15  A    C
ATOM   3239  CE3 TRP A 616      20.306  -3.896  18.799  1.00  7.66           A    C
ANISOU 3239  CE3 TRP A 616     968   1061    880    103     17    -50  A    C
ATOM   3241  CZ3 TRP A 616      21.347  -3.004  18.624  1.00  9.44           A    C
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ANISOU 3241  CZ3 TRP A 616     1356   1158   1072    -34     44    -11  A    C
ATOM   3243  CH2 TRP A 616      22.699  -3.455  18.561  1.00  9.10       A    C
ANISOU 3243  CH2 TRP A 616     1173   1093   1191   -100    118     41  A    C
ATOM   3245  CZ2 TRP A 616      23.013  -4.792  18.688  1.00  7.47       A    C
ANISOU 3245  CZ2 TRP A 616      796   1171    872    140    -57    103  A    C
ATOM   3247  C   TRP A 616      18.191  -4.868  21.202  1.00  8.49       A    C
ANISOU 3247  C   TRP A 616     1121   1094   1010     27      0    -16  A    C
ATOM   3248  O   TRP A 616      19.128  -4.740  22.001  1.00  8.40       A    O
ANISOU 3248  O   TRP A 616     1102   1097    992     48    -62    -44  A    O
ATOM   3249  N   GLU A 617      17.446  -3.846  20.808  1.00  8.56       A    N
ANISOU 3249  N   GLU A 617     1104   1176    972     26     55    -50  A    N
ATOM   3251  CA  GLU A 617      17.707  -2.480  21.291  1.00  8.72       A    C
ANISOU 3251  CA  GLU A 617     1138   1122   1049    -19     34    -30  A    C
ATOM   3253  CB  GLU A 617      16.741  -1.474  20.683  1.00 10.12       A    C
ANISOU 3253  CB  GLU A 617     1364   1194   1286     37     13    -31  A    C
ATOM   3256  CG  GLU A 617      16.935  -1.149  19.226  1.00 10.89       A    C
ANISOU 3256  CG  GLU A 617     1363   1413   1358     41      5     -6  A    C
ATOM   3259  CD  GLU A 617      15.885  -0.160  18.752  1.00 10.67       A    C
ANISOU 3259  CD  GLU A 617     1444   1309   1300    -64    -98    -28  A    C
ATOM   3260  OE1 GLU A 617      14.700  -0.467  18.885  1.00 12.97       A    O
ANISOU 3260  OE1 GLU A 617     1515   1667   1743     56      0    -36  A    O
ATOM   3261  OE2 GLU A 617      16.235   0.929  18.273  1.00 13.44       A    O
ANISOU 3261  OE2 GLU A 617     2111   1387   1607    143     94    261  A    O
ATOM   3262  C   GLU A 617      17.546  -2.389  22.804  1.00  8.46       A    C
ANISOU 3262  C   GLU A 617     1032   1175   1004    -33     47    -43  A    C
ATOM   3263  O   GLU A 617      18.366  -1.773  23.498  1.00  8.69       A    O
ANISOU 3263  O   GLU A 617     1089   1238    973    -65     19    -75  A    O
ATOM   3264  N   ILE A 618      16.478  -2.991  23.316  1.00  7.97       A    N
ANISOU 3264  N   ILE A 618     1115    965    946    -34     38    -41  A    N
ATOM   3266  CA  ILE A 618      16.230  -2.950  24.766  1.00  7.93       A    C
ANISOU 3266  CA  ILE A 618     1051   1005    955     76     27     30  A    C
ATOM   3268  CB  ILE A 618      14.879  -3.602  25.083  1.00  8.25       A    C
ANISOU 3268  CB  ILE A 618     1131   1002    999     60     26      0  A    C
ATOM   3270  CG1 ILE A 618      13.748  -2.752  24.464  1.00  8.51       A    C
ANISOU 3270  CG1 ILE A 618     1117   1100   1015      5     58     97  A    C
ATOM   3273  CD1 ILE A 618      12.366  -3.346  24.595  1.00  9.45       A    C
ANISOU 3273  CD1 ILE A 618     1179   1134   1277     53    148     10  A    C
ATOM   3277  CG2 ILE A 618      14.706  -3.777  26.605  1.00  8.97       A    C
ANISOU 3277  CG2 ILE A 618     1159   1211   1036     90     40     53  A    C
ATOM   3281  C   ILE A 618      17.389  -3.599  25.542  1.00  8.12       A    C
ANISOU 3281  C   ILE A 618      994   1054   1038    -19     -3    -40  A    C
ATOM   3282  O   ILE A 618      17.924  -3.029  26.507  1.00  8.54       A    O
ANISOU 3282  O   ILE A 618     1122   1077   1044     -1     97    -32  A    O
ATOM   3283  N   LEU A 619      17.755  -4.815  25.110  1.00  8.06       A    N
ANISOU 3283  N   LEU A 619     1022   1042    997     56    -64      4  A    N
ATOM   3285  CA  LEU A 619      18.817  -5.570  25.803  1.00  9.30       A    C
ANISOU 3285  CA  LEU A 619     1150   1164   1217     24    -21     18  A    C
ATOM   3287  CB  LEU A 619      18.771  -7.042  25.366  1.00  9.66       A    C
ANISOU 3287  CB  LEU A 619     1250   1206   1214     38    -46    -39  A    C
ATOM   3290  CG  LEU A 619      17.852  -7.985  26.156  1.00 10.45       A    C
ANISOU 3290  CG  LEU A 619     1313   1244   1411     25     23    -73  A    C
ATOM   3292  CD1 LEU A 619      18.316  -8.193  27.599  1.00 11.33       A    C
ANISOU 3292  CD1 LEU A 619     1599   1208   1496     98     55     23  A    C
ATOM   3296  CD2 LEU A 619      16.378  -7.523  26.133  1.00 10.51       A    C
ANISOU 3296  CD2 LEU A 619     1328   1153   1509     53    -27     19  A    C
ATOM   3300  C   LEU A 619      20.193  -4.965  25.575  1.00  8.94       A    C
ANISOU 3300  C   LEU A 619     1136   1142   1118     63    -19    -31  A    C
ATOM   3301  O   LEU A 619      21.121  -5.297  26.290  1.00 10.08       A    O
ANISOU 3301  O   LEU A 619     1381   1287   1162     56   -119     -2  A    O
ATOM   3302  N   SER A 620      20.296  -4.033  24.631  1.00  8.88       A    N
ANISOU 3302  N   SER A 620     1103   1151   1117     -3    -50     13  A    N
ATOM   3304  CA  SER A 620      21.505  -3.261  24.373  1.00  9.66       A    C
ANISOU 3304  CA  SER A 620     1202   1184   1282     53      8     10  A    C
ATOM   3306  CB  SER A 620      21.728  -3.183  22.869  1.00  9.29       A    C
ANISOU 3306  CB  SER A 620     1200   1104   1224     49     -5    -98  A    C
ATOM   3309  OG  SER A 620      21.807  -4.470  22.292  1.00 10.72       A    O
ANISOU 3309  OG  SER A 620     1387   1338   1346     65    -36   -323  A    O
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ATOM   3311  C   SER A 620      21.456  -1.832  24.937  1.00  9.21           A    C
ANISOU 3311  C   SER A 620    1174   1196   1129    -50     35    -27  A    C
ATOM   3312  O   SER A 620      22.307  -1.008  24.608  1.00 11.06           A    O
ANISOU 3312  O   SER A 620    1474   1382   1344   -139     85     -4  A    O
ATOM   3313  N   PHE A 621      20.462  -1.529  25.771  1.00  8.95           A    N
ANISOU 3313  N   PHE A 621    1114   1132   1155    -23     27    -28  A    N
ATOM   3315  CA  PHE A 621      20.337  -0.218  26.387  1.00  9.65           A    C
ANISOU 3315  CA  PHE A 621    1236   1282   1145     46     20    -98  A    C
ATOM   3317  CB  PHE A 621      21.468   0.011  27.414  1.00 10.29           A    C
ANISOU 3317  CB  PHE A 621    1288   1375   1245      0      3    -64  A    C
ATOM   3320  CG  PHE A 621      21.477  -1.003  28.516  1.00  9.62           A    C
ANISOU 3320  CG  PHE A 621    1337   1174   1142    -58    -37    -88  A    C
ATOM   3321  CD1 PHE A 621      20.646  -0.866  29.598  1.00 11.01           A    C
ANISOU 3321  CD1 PHE A 621    1456   1403   1323      1     25    -48  A    C
ATOM   3323  CE1 PHE A 621      20.632  -1.815  30.628  1.00 11.66           A    C
ANISOU 3323  CE1 PHE A 621    1557   1483   1388     11      4      6  A    C
ATOM   3325  CZ  PHE A 621      21.478  -2.876  30.576  1.00 12.92           A    C
ANISOU 3325  CZ  PHE A 621    1757   1692   1458    113    121     56  A    C
ATOM   3327  CE2 PHE A 621      22.325  -3.025  29.477  1.00 14.15           A    C
ANISOU 3327  CE2 PHE A 621    1903   1798   1672    126    166     30  A    C
ATOM   3329  CD2 PHE A 621      22.320  -2.086  28.478  1.00 11.25           A    C
ANISOU 3329  CD2 PHE A 621    1501   1547   1223     98     92    -83  A    C
ATOM   3331  C   PHE A 621      20.241   0.921  25.373  1.00 10.39           A    C
ANISOU 3331  C   PHE A 621    1360   1302   1286     22     -4    -79  A    C
ATOM   3332  O   PHE A 621      20.786   2.011  25.569  1.00 11.34           A    O
ANISOU 3332  O   PHE A 621    1621   1375   1311     32    -13   -117  A    O
ATOM   3333  N   GLY A 622      19.522   0.651  24.285  1.00 11.10           A    N
ANISOU 3333  N   GLY A 622    1512   1375   1328     42    -63    -81  A    N
ATOM   3335  CA  GLY A 622      19.193   1.662  23.303  1.00 11.22           A    C
ANISOU 3335  CA  GLY A 622    1468   1417   1376     66      4    -22  A    C
ATOM   3338  C   GLY A 622      20.124   1.861  22.126  1.00 12.73           A    C
ANISOU 3338  C   GLY A 622    1686   1597   1551     18     20    -39  A    C
ATOM   3339  O   GLY A 622      19.920   2.776  21.338  1.00 14.16           A    O
ANISOU 3339  O   GLY A 622    1927   1912   1540    219    -37    -18  A    O
ATOM   3340  N   LYS A 623      21.153   1.030  21.998  1.00 12.99           A    N
ANISOU 3340  N   LYS A 623    1681   1643   1610     69    -29    -17  A    N
ATOM   3342  CA  LYS A 623      22.031   1.135  20.830  1.00 14.46           A    C
ANISOU 3342  CA  LYS A 623    1800   1899   1795      0     -6    -28  A    C
ATOM   3344  CB  LYS A 623      23.171   0.133  20.897  1.00 16.42           A    C
ANISOU 3344  CB  LYS A 623    2096   2093   2050     76      2      5  A    C
ATOM   3347  CG  LYS A 623      24.168   0.387  22.051  1.00 19.39           A    C
ANISOU 3347  CG  LYS A 623    2346   2627   2395     31    -71    -13  A    C
ATOM   3350  CD  LYS A 623      24.349   1.876  22.432  1.00 23.86           A    C
ANISOU 3350  CD  LYS A 623    3111   2953   2998    -20    -35    -29  A    C
ATOM   3353  CE  LYS A 623      25.567   2.118  23.318  1.00 25.46           A    C
ANISOU 3353  CE  LYS A 623    3218   3278   3177      8    -71     33  A    C
ATOM   3356  NZ  LYS A 623      25.748   3.571  23.628  1.00 27.42           A    N
ANISOU 3356  NZ  LYS A 623    3624   3417   3377    -57    -46    -49  A    N
ATOM   3360  C   LYS A 623      21.255   0.917  19.534  1.00 13.13           A    C
ANISOU 3360  C   LYS A 623    1680   1666   1643     49     26    -50  A    C
ATOM   3361  O   LYS A 623      20.255   0.223  19.513  1.00 12.72           A    O
ANISOU 3361  O   LYS A 623    1567   1670   1594     15    118   -135  A    O
ATOM   3362  N   GLN A 624      21.722   1.549  18.473  1.00 12.29           A    N
ANISOU 3362  N   GLN A 624    1579   1448   1640      9     21    -24  A    N
ATOM   3364  CA  GLN A 624      21.102   1.440  17.176  1.00 12.12           A    C
ANISOU 3364  CA  GLN A 624    1546   1487   1573     20     19     -7  A    C
ATOM   3366  CB  GLN A 624      21.541   2.586  16.243  1.00 13.32           A    C
ANISOU 3366  CB  GLN A 624    1719   1539   1803     31     66     15  A    C
ATOM   3369  CG  GLN A 624      20.909   2.482  14.840  1.00 18.07           A    C
ANISOU 3369  CG  GLN A 624    2357   2269   2240     73    -72    -62  A    C
ATOM   3372  CD  GLN A 624      21.509   3.377  13.743  1.00 22.31           A    C
ANISOU 3372  CD  GLN A 624    2878   2762   2837    -40     63     88  A    C
ATOM   3373  OE1 GLN A 624      22.588   3.095  13.196  1.00 24.31           A    O
ANISOU 3373  OE1 GLN A 624    2960   3051   3224     92      9    132  A    O
ATOM   3374  NE2 GLN A 624      20.752   4.398  13.348  1.00 26.33           A    N
ANISOU 3374  NE2 GLN A 624    3465   3053   3484    164     -3     82  A    N
ATOM   3377  C   GLN A 624      21.489   0.123  16.542  1.00 10.73           A    C
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ANISOU 3377  C   GLN A 624     1339   1325   1410     -9     -7     41  A    C
ATOM   3378  O   GLN A 624      22.681  -0.206  16.488  1.00 10.29      A    O
ANISOU 3378  O   GLN A 624     1224   1167   1518    -91     43    -37  A    O
ATOM   3379  N   PRO A 625      20.516  -0.603  16.000  1.00  9.27      A    N
ANISOU 3379  N   PRO A 625     1193   1126   1200    -19     20    -26  A    N
ATOM   3380  CA  PRO A 625      20.831  -1.847  15.293  1.00  9.00      A    C
ANISOU 3380  CA  PRO A 625     1099   1095   1224     57     50     15  A    C
ATOM   3382  CB  PRO A 625      19.456  -2.402  14.917  1.00  8.99      A    C
ANISOU 3382  CB  PRO A 625     1186   1082   1145     35     24     46  A    C
ATOM   3385  CG  PRO A 625      18.570  -1.210  14.867  1.00  9.14      A    C
ANISOU 3385  CG  PRO A 625     1226   1066   1180     86    122     46  A    C
ATOM   3388  CD  PRO A 625      19.069  -0.317  15.969  1.00  9.56      A    C
ANISOU 3388  CD  PRO A 625     1275   1169   1187     34     53    105  A    C
ATOM   3391  C   PRO A 625      21.685  -1.542  14.067  1.00  8.92      A    C
ANISOU 3391  C   PRO A 625     1173   1016   1200     25     48     54  A    C
ATOM   3392  O   PRO A 625      21.435  -0.568  13.358  1.00  9.28      A    O
ANISOU 3392  O   PRO A 625     1224   1087   1215     71     94    122  A    O
ATOM   3393  N   PHE A 626      22.701  -2.370  13.815  1.00  7.60      A    N
ANISOU 3393  N   PHE A 626      936    903   1048     19    -50     11  A    N
ATOM   3395  CA  PHE A 626      23.534  -2.225  12.629  1.00  7.73      A    C
ANISOU 3395  CA  PHE A 626     1076    877    982     12    -48     21  A    C
ATOM   3397  CB  PHE A 626      22.737  -2.566  11.356  1.00  7.40      A    C
ANISOU 3397  CB  PHE A 626     1034    884    894     -3      5    -12  A    C
ATOM   3400  CG  PHE A 626      22.329  -4.021  11.255  1.00  8.09      A    C
ANISOU 3400  CG  PHE A 626     1041   1024   1008    -86     -2    -46  A    C
ATOM   3401  CD1 PHE A 626      23.294  -5.024  11.215  1.00  7.67      A    C
ANISOU 3401  CD1 PHE A 626     1036    890    988   -162   -239     27  A    C
ATOM   3403  CE1 PHE A 626      22.924  -6.362  11.159  1.00  8.27      A    C
ANISOU 3403  CE1 PHE A 626     1141    784   1216     93     -7    -18  A    C
ATOM   3405  CZ  PHE A 626      21.587  -6.709  11.106  1.00  8.76      A    C
ANISOU 3405  CZ  PHE A 626     1255    969   1101    -52    -21   -137  A    C
ATOM   3407  CE2 PHE A 626      20.608  -5.726  11.146  1.00  7.41      A    C
ANISOU 3407  CE2 PHE A 626      984   1007    823   -114     46      0  A    C
ATOM   3409  CD2 PHE A 626      20.983  -4.378  11.219  1.00  8.31      A    C
ANISOU 3409  CD2 PHE A 626     1055   1051   1049    -57      4     28  A    C
ATOM   3411  C   PHE A 626      24.146  -0.827  12.547  1.00  8.26      A    C
ANISOU 3411  C   PHE A 626     1166    926   1043     37    -49     14  A    C
ATOM   3412  O   PHE A 626      24.344  -0.279  11.477  1.00  8.99      A    O
ANISOU 3412  O   PHE A 626     1258    970   1188     51     -9    -20  A    O
ATOM   3413  N   PHE A 627      24.528  -0.292  13.699  1.00  8.24      A    N
ANISOU 3413  N   PHE A 627     1259    876    995     -4    -74     26  A    N
ATOM   3415  CA  PHE A 627      25.174   1.024  13.707  1.00  9.11      A    C
ANISOU 3415  CA  PHE A 627     1240   1060   1159    -58    -25    -17  A    C
ATOM   3417  CB  PHE A 627      25.424   1.511  15.140  1.00  9.32      A    C
ANISOU 3417  CB  PHE A 627     1293   1146   1103    -79    -39    -37  A    C
ATOM   3420  CG  PHE A 627      26.369   0.645  15.944  1.00  9.19      A    C
ANISOU 3420  CG  PHE A 627     1223   1095   1172    -86    -26    -71  A    C
ATOM   3421  CD1 PHE A 627      27.735   0.787  15.834  1.00 10.25      A    C
ANISOU 3421  CD1 PHE A 627     1241   1227   1427     -6    -56   -130  A    C
ATOM   3423  CE1 PHE A 627      28.598  -0.008  16.569  1.00  9.28      A    C
ANISOU 3423  CE1 PHE A 627     1125   1270   1131   -139    -83     -7  A    C
ATOM   3425  CZ  PHE A 627      28.106  -0.937  17.430  1.00 10.17      A    C
ANISOU 3425  CZ  PHE A 627     1354   1332   1178     51    -91     64  A    C
ATOM   3427  CE2 PHE A 627      26.740  -1.080  17.553  1.00 10.61      A    C
ANISOU 3427  CE2 PHE A 627     1444   1401   1183    -72    -11    -72  A    C
ATOM   3429  CD2 PHE A 627      25.893  -0.299  16.833  1.00  8.87      A    C
ANISOU 3429  CD2 PHE A 627     1305   1018   1045   -100      9   -208  A    C
ATOM   3431  C   PHE A 627      26.456   1.077  12.892  1.00 10.08      A    C
ANISOU 3431  C   PHE A 627     1346   1201   1281    -68      0     23  A    C
ATOM   3432  O   PHE A 627      26.887   2.177  12.510  1.00 11.98      A    O
ANISOU 3432  O   PHE A 627     1683   1284   1583   -151     37     95  A    O
ATOM   3433  N   TRP A 628      27.053  -0.093  12.649  1.00 10.14      A    N
ANISOU 3433  N   TRP A 628     1228   1310   1315    -37     -3     -3  A    N
ATOM   3435  CA  TRP A 628      28.347  -0.244  11.983  1.00 11.50      A    C
ANISOU 3435  CA  TRP A 628     1418   1502   1446    -38     19      8  A    C
ATOM   3437  CB  TRP A 628      29.083  -1.495  12.512  1.00 11.81      A    C
ANISOU 3437  CB  TRP A 628     1473   1562   1452     21     -8     -3  A    C
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ATOM   3440  CG  TRP A 628      28.265  -2.820  12.467  1.00 11.23           A    C
ANISOU 3440  CG  TRP A 628     1405   1410   1451     93    -65    -64  A    C
ATOM   3441  CD1 TRP A 628      28.293  -3.793  11.476  1.00 11.11           A    C
ANISOU 3441  CD1 TRP A 628     1339   1477   1406    170   -262    -42  A    C
ATOM   3443  NE1 TRP A 628      27.423  -4.809  11.789  1.00 12.58           A    N
ANISOU 3443  NE1 TRP A 628     1741   1422   1616    220   -272     -9  A    N
ATOM   3445  CE2 TRP A 628      26.795  -4.531  12.966  1.00 11.44           A    C
ANISOU 3445  CE2 TRP A 628     1445   1326   1572    113   -268    136  A    C
ATOM   3446  CD2 TRP A 628      27.306  -3.277  13.427  1.00 10.60           A    C
ANISOU 3446  CD2 TRP A 628     1462   1248   1315      0   -261     72  A    C
ATOM   3447  CE3 TRP A 628      26.816  -2.770  14.624  1.00 10.04           A    C
ANISOU 3447  CE3 TRP A 628     1218   1287   1308    100   -209     58  A    C
ATOM   3449  CZ3 TRP A 628      25.850  -3.499  15.329  1.00 11.14           A    C
ANISOU 3449  CZ3 TRP A 628     1512   1390   1329    -80   -227    -54  A    C
ATOM   3451  CH2 TRP A 628      25.372  -4.727  14.846  1.00 12.39           A    C
ANISOU 3451  CH2 TRP A 628     1663   1370   1675     -8   -202     -3  A    C
ATOM   3453  CZ2 TRP A 628      25.848  -5.260  13.680  1.00 10.83           A    C
ANISOU 3453  CZ2 TRP A 628     1406   1287   1419     60   -245     50  A    C
ATOM   3455  C   TRP A 628      28.219  -0.323  10.460  1.00 12.25           A    C
ANISOU 3455  C   TRP A 628     1482   1674   1495    -25     19     22  A    C
ATOM   3456  O   TRP A 628      29.234  -0.395   9.757  1.00 14.02           A    O
ANISOU 3456  O   TRP A 628     1642   2078   1606      7     63     11  A    O
ATOM   3457  N   LEU A 629      26.980  -0.302   9.964  1.00 12.51           A    N
ANISOU 3457  N   LEU A 629     1535   1705   1512    -32    -17     29  A    N
ATOM   3459  CA  LEU A 629      26.669  -0.380   8.536  1.00 12.79           A    C
ANISOU 3459  CA  LEU A 629     1617   1700   1542    -32     11      7  A    C
ATOM   3461  CB  LEU A 629      25.702  -1.541   8.289  1.00 12.60           A    C
ANISOU 3461  CB  LEU A 629     1610   1647   1529    -14     -9    -14  A    C
ATOM   3464  CG  LEU A 629      26.137  -2.945   8.678  1.00 12.33           A    C
ANISOU 3464  CG  LEU A 629     1646   1651   1386     14    -97     -1  A    C
ATOM   3466  CD1 LEU A 629      25.054  -3.913   8.301  1.00 13.38           A    C
ANISOU 3466  CD1 LEU A 629     1752   1716   1614    -33     -6     93  A    C
ATOM   3470  CD2 LEU A 629      27.422  -3.323   8.009  1.00 13.37           A    C
ANISOU 3470  CD2 LEU A 629     1713   1765   1599     56    -77      0  A    C
ATOM   3474  C   LEU A 629      25.978   0.881   8.034  1.00 13.68           A    C
ANISOU 3474  C   LEU A 629     1762   1761   1673      5      7     25  A    C
ATOM   3475  O   LEU A 629      25.349   1.609   8.806  1.00 14.67           A    O
ANISOU 3475  O   LEU A 629     2007   1915   1652     56     17    146  A    O
ATOM   3476  N   GLU A 630      26.047   1.100   6.723  1.00 15.20           A    N
ANISOU 3476  N   GLU A 630     1933   1972   1868    -43     19     53  A    N
ATOM   3478  CA  GLU A 630      25.195   2.078   6.050  1.00 15.90           A    C
ANISOU 3478  CA  GLU A 630     2047   2013   1981    -18    -32     34  A    C
ATOM   3480  CB  GLU A 630      25.887   2.644   4.805  1.00 16.75           A    C
ANISOU 3480  CB  GLU A 630     2158   2129   2076    -24     14     48  A    C
ATOM   3483  CG  GLU A 630      27.081   3.540   5.068  1.00 19.59           A    C
ANISOU 3483  CG  GLU A 630     2476   2449   2518    -38    -51    -29  A    C
ATOM   3486  CD  GLU A 630      27.635   4.127   3.778  1.00 23.92           A    C
ANISOU 3486  CD  GLU A 630     3112   3047   2928    -45     50     79  A    C
ATOM   3487  OE1 GLU A 630      28.396   3.432   3.073  1.00 25.66           A    O
ANISOU 3487  OE1 GLU A 630     3327   3302   3119     51    180     61  A    O
ATOM   3488  OE2 GLU A 630      27.278   5.275   3.454  1.00 27.92           A    O
ANISOU 3488  OE2 GLU A 630     3780   3258   3571     71    -64     56  A    O
ATOM   3489  C   GLU A 630      23.916   1.364   5.631  1.00 15.32           A    C
ANISOU 3489  C   GLU A 630     1983   1960   1875      0    -57     56  A    C
ATOM   3490  O   GLU A 630      23.947   0.155   5.409  1.00 14.36           A    O
ANISOU 3490  O   GLU A 630     1855   1857   1744    -22   -239     28  A    O
ATOM   3491  N   ASN A 631      22.802   2.095   5.510  1.00 15.10           A    N
ANISOU 3491  N   ASN A 631     2014   1832   1889    -11    -36     32  A    N
ATOM   3493  CA  ASN A 631      21.527   1.489   5.144  1.00 15.38           A    C
ANISOU 3493  CA  ASN A 631     2016   1916   1909      9    -24     57  A    C
ATOM   3495  CB  ASN A 631      20.452   2.554   4.851  1.00 15.89           A    C
ANISOU 3495  CB  ASN A 631     2019   2001   2014     42    -89     39  A    C
ATOM   3498  CG  ASN A 631      19.746   3.067   6.094  1.00 16.81           A    C
ANISOU 3498  CG  ASN A 631     2269   2093   2023     68    -85     65  A    C
ATOM   3499  OD1 ASN A 631      19.985   2.593   7.216  1.00 16.14           A    O
ANISOU 3499  OD1 ASN A 631     2243   1942   1945     23    -77    176  A    O
ATOM   3500  ND2 ASN A 631      18.830   4.050   5.900  1.00 18.61           A    N
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ANISOU 3500  ND2 ASN A 631     2402   2304   2362    141    -75    -12  A    N
ATOM   3503  C   ASN A 631      21.653   0.574   3.941  1.00 15.25        A    C
ANISOU 3503  C   ASN A 631     1952   1921   1919      9    -14     43  A    C
ATOM   3504  O   ASN A 631      21.066  -0.496   3.911  1.00 14.96        A    O
ANISOU 3504  O   ASN A 631     2104   1781   1796    -12    -27     63  A    O
ATOM   3505  N   LYS A 632      22.393   1.018   2.931  1.00 15.71        A    N
ANISOU 3505  N   LYS A 632     2046   1977   1945    -22    -23     79  A    N
ATOM   3507  CA  LYS A 632      22.511   0.279   1.674  1.00 16.46        A    C
ANISOU 3507  CA  LYS A 632     2123   2082   2048    -14     -5     15  A    C
ATOM   3509  CB  LYS A 632      23.235   1.134   0.605  1.00 17.14        A    C
ANISOU 3509  CB  LYS A 632     2275   2140   2096    -11    -14     60  A    C
ATOM   3512  CG  LYS A 632      24.720   1.347   0.845  1.00 19.38        A    C
ANISOU 3512  CG  LYS A 632     2408   2456   2498    -32    -13     48  A    C
ATOM   3515  CD  LYS A 632      25.458   1.946  -0.371  1.00 22.31        A    C
ANISOU 3515  CD  LYS A 632     2923   2801   2751    -20     62     44  A    C
ATOM   3518  CE  LYS A 632      26.963   2.027  -0.095  1.00 24.58        A    C
ANISOU 3518  CE  LYS A 632     3082   3122   3135    -35    -23     27  A    C
ATOM   3521  NZ  LYS A 632      27.705   2.894  -1.061  1.00 26.47        A    N
ANISOU 3521  NZ  LYS A 632     3387   3352   3317    -17     57     30  A    N
ATOM   3525  C   LYS A 632      23.194  -1.074   1.833  1.00 15.77        A    C
ANISOU 3525  C   LYS A 632     2016   2031   1942    -32    -13     24  A    C
ATOM   3526  O   LYS A 632      23.051  -1.953   0.996  1.00 16.37        A    O
ANISOU 3526  O   LYS A 632     2199   2170   1850    -15    -30      7  A    O
ATOM   3527  N   ASP A 633      23.937  -1.253   2.919  1.00 15.01        A    N
ANISOU 3527  N   ASP A 633     1921   1944   1836    -26     -3    -10  A    N
ATOM   3529  CA  ASP A 633      24.661  -2.493   3.139  1.00 15.01        A    C
ANISOU 3529  CA  ASP A 633     1895   1914   1893    -22      0      8  A    C
ATOM   3531  CB  ASP A 633      25.958  -2.190   3.882  1.00 16.28        A    C
ANISOU 3531  CB  ASP A 633     2051   2039   2095     19    -82    -21  A    C
ATOM   3534  CG  ASP A 633      27.019  -1.561   2.966  1.00 19.59        A    C
ANISOU 3534  CG  ASP A 633     2490   2424   2529    -40     98     35  A    C
ATOM   3535  OD1 ASP A 633      26.772  -1.374   1.760  1.00 24.84        A    O
ANISOU 3535  OD1 ASP A 633     3235   3123   3080     -1   -125    185  A    O
ATOM   3536  OD2 ASP A 633      28.154  -1.266   3.350  1.00 24.27        A    O
ANISOU 3536  OD2 ASP A 633     3011   3068   3140   -140    -93    -75  A    O
ATOM   3537  C   ASP A 633      23.869  -3.555   3.896  1.00 13.27        A    C
ANISOU 3537  C   ASP A 633     1660   1734   1647     14    -30    -24  A    C
ATOM   3538  O   ASP A 633      24.270  -4.711   3.936  1.00 13.66        A    O
ANISOU 3538  O   ASP A 633     1712   1795   1680      2      7    -23  A    O
ATOM   3539  N   VAL A 634      22.737  -3.157   4.479  1.00 11.49        A    N
ANISOU 3539  N   VAL A 634     1423   1491   1453    -26    -28      5  A    N
ATOM   3541  CA  VAL A 634      22.008  -4.016   5.386  1.00 11.05        A    C
ANISOU 3541  CA  VAL A 634     1405   1454   1337     -5    -35     15  A    C
ATOM   3543  CB  VAL A 634      20.863  -3.256   6.056  1.00 10.53        A    C
ANISOU 3543  CB  VAL A 634     1351   1365   1282    -33    -39     64  A    C
ATOM   3545  CG1 VAL A 634      19.950  -4.217   6.852  1.00 11.29        A    C
ANISOU 3545  CG1 VAL A 634     1363   1582   1344    -27    121     -4  A    C
ATOM   3549  CG2 VAL A 634      21.388  -2.174   6.941  1.00 11.26        A    C
ANISOU 3549  CG2 VAL A 634     1398   1428   1451   -153     96     81  A    C
ATOM   3553  C   VAL A 634      21.481  -5.264   4.685  1.00 11.12        A    C
ANISOU 3553  C   VAL A 634     1404   1453   1366    -12      0     35  A    C
ATOM   3554  O   VAL A 634      21.681  -6.371   5.174  1.00 10.89        A    O
ANISOU 3554  O   VAL A 634     1296   1492   1349    105     72    -22  A    O
ATOM   3555  N   ILE A 635      20.816  -5.099   3.542  1.00 11.18        A    N
ANISOU 3555  N   ILE A 635     1387   1435   1424    -49      3     64  A    N
ATOM   3557  CA  ILE A 635      20.221  -6.252   2.891  1.00 11.30        A    C
ANISOU 3557  CA  ILE A 635     1393   1486   1414    -12    -41     17  A    C
ATOM   3559  CB  ILE A 635      19.316  -5.847   1.719  1.00 11.18        A    C
ANISOU 3559  CB  ILE A 635     1329   1472   1444     22    -10     -5  A    C
ATOM   3561  CG1 ILE A 635      18.478  -7.053   1.270  1.00 11.96        A    C
ANISOU 3561  CG1 ILE A 635     1556   1507   1479    -27    -47    -50  A    C
ATOM   3564  CD1 ILE A 635      17.492  -7.555   2.279  1.00 12.52        A    C
ANISOU 3564  CD1 ILE A 635     1484   1578   1694     60      9      4  A    C
ATOM   3568  CG2 ILE A 635      20.115  -5.305   0.563  1.00 11.86        A    C
ANISOU 3568  CG2 ILE A 635     1484   1608   1413    -28    -68     47  A    C
ATOM   3572  C   ILE A 635      21.259  -7.287   2.498  1.00 11.28        A    C
ANISOU 3572  C   ILE A 635     1409   1464   1412    -25    -34     24  A    C
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ATOM   3573  O   ILE A 635      21.030  -8.481   2.660  1.00 11.42           A    O
ANISOU 3573  O   ILE A 635    1400   1440   1496     -7   -159    -55  A    O
ATOM   3574  N   GLY A 636      22.426  -6.844   2.046  1.00 11.85           A    N
ANISOU 3574  N   GLY A 636    1458   1484   1560    -12    -25     23  A    N
ATOM   3576  CA  GLY A 636      23.473  -7.790   1.712  1.00 12.18           A    C
ANISOU 3576  CA  GLY A 636    1507   1563   1556    -13     47      8  A    C
ATOM   3579  C   GLY A 636      23.909  -8.641   2.891  1.00 12.11           A    C
ANISOU 3579  C   GLY A 636    1509   1531   1561     -1     38      0  A    C
ATOM   3580  O   GLY A 636      24.137  -9.842   2.762  1.00 12.65           A    O
ANISOU 3580  O   GLY A 636    1609   1535   1661     33     39    -14  A    O
ATOM   3581  N   VAL A 637      24.021  -8.013   4.054  1.00 11.63           A    N
ANISOU 3581  N   VAL A 637    1400   1458   1560     39      9    -25  A    N
ATOM   3583  CA  VAL A 637      24.420  -8.698   5.273  1.00 11.85           A    C
ANISOU 3583  CA  VAL A 637    1469   1539   1494     20     59    -35  A    C
ATOM   3585  CB  VAL A 637      24.685  -7.642   6.391  1.00 12.84           A    C
ANISOU 3585  CB  VAL A 637    1581   1614   1682     10    -46    -47  A    C
ATOM   3587  CG1 VAL A 637      24.600  -8.211   7.750  1.00 15.93           A    C
ANISOU 3587  CG1 VAL A 637    2107   2036   1909    -28    -36    -64  A    C
ATOM   3591  CG2 VAL A 637      26.022  -6.963   6.152  1.00 14.08           A    C
ANISOU 3591  CG2 VAL A 637    1825   1719   1805    -80     21    -75  A    C
ATOM   3595  C   VAL A 637      23.338  -9.723   5.662  1.00 10.63           A    C
ANISOU 3595  C   VAL A 637    1337   1366   1333     20      0    -35  A    C
ATOM   3596  O   VAL A 637      23.611 -10.862   5.976  1.00 11.17           A    O
ANISOU 3596  O   VAL A 637    1276   1517   1451    100     18   -115  A    O
ATOM   3597  N   LEU A 638      22.079  -9.325   5.619  1.00 10.88           A    N
ANISOU 3597  N   LEU A 638    1352   1350   1431     35     24    -43  A    N
ATOM   3599  CA  LEU A 638      21.002 -10.244   5.992  1.00 11.05           A    C
ANISOU 3599  CA  LEU A 638    1461   1375   1361    -15     40    -26  A    C
ATOM   3601  CB  LEU A 638      19.658  -9.521   6.027  1.00 10.68           A    C
ANISOU 3601  CB  LEU A 638    1429   1309   1320     -3     35    -22  A    C
ATOM   3604  CG  LEU A 638      19.547  -8.344   7.011  1.00 10.27           A    C
ANISOU 3604  CG  LEU A 638    1344   1282   1277    -76     -1     -7  A    C
ATOM   3606  CD1 LEU A 638      18.238  -7.630   6.794  1.00  9.53           A    C
ANISOU 3606  CD1 LEU A 638    1420   1197   1003    -27     87    -76  A    C
ATOM   3610  CD2 LEU A 638      19.732  -8.792   8.440  1.00 10.25           A    C
ANISOU 3610  CD2 LEU A 638    1304   1365   1226    -26    -11    -46  A    C
ATOM   3614  C   LEU A 638      20.915 -11.413   5.013  1.00 11.41           A    C
ANISOU 3614  C   LEU A 638    1477   1379   1478     10     57    -50  A    C
ATOM   3615  O   LEU A 638      20.712 -12.537   5.423  1.00 10.84           A    O
ANISOU 3615  O   LEU A 638    1420   1333   1364    -17    123   -103  A    O
ATOM   3616  N   GLU A 639      21.083 -11.132   3.727  1.00 12.44           A    N
ANISOU 3616  N   GLU A 639    1656   1525   1545    -42     27    -63  A    N
ATOM   3618  CA  GLU A 639      21.074 -12.190   2.705  1.00 13.00           A    C
ANISOU 3618  CA  GLU A 639    1690   1632   1615    -14     32    -62  A    C
ATOM   3620  CB  GLU A 639      21.095 -11.605   1.273  1.00 14.26           A    C
ANISOU 3620  CB  GLU A 639    1957   1762   1696    -36     34    -66  A    C
ATOM   3623  CG  GLU A 639      19.797 -10.934   0.839  1.00 17.67           A    C
ANISOU 3623  CG  GLU A 639    2268   2152   2291     24    -11    -51  A    C
ATOM   3626  CD  GLU A 639      19.890 -10.273  -0.542  1.00 22.72           A    C
ANISOU 3626  CD  GLU A 639    3100   2823   2708     21      0     24  A    C
ATOM   3627  OE1 GLU A 639      21.009 -10.130  -1.081  1.00 26.70           A    O
ANISOU 3627  OE1 GLU A 639    3484   3423   3237    -81    115     45  A    O
ATOM   3628  OE2 GLU A 639      18.840  -9.871  -1.079  1.00 26.87           A    O
ANISOU 3628  OE2 GLU A 639    3480   3331   3398     42   -197     -6  A    O
ATOM   3629  C   GLU A 639      22.216 -13.185   2.917  1.00 13.08           A    C
ANISOU 3629  C   GLU A 639    1741   1634   1594    -12     -4    -48  A    C
ATOM   3630  O   GLU A 639      22.049 -14.344   2.645  1.00 13.54           A    O
ANISOU 3630  O   GLU A 639    1800   1633   1712      1    -38    -82  A    O
ATOM   3631  N   LYS A 640      23.359 -12.742   3.442  1.00 12.74           A    N
ANISOU 3631  N   LYS A 640    1633   1625   1583      1     16    -74  A    N
ATOM   3633  CA  LYS A 640      24.478 -13.640   3.735  1.00 13.77           A    C
ANISOU 3633  CA  LYS A 640    1810   1698   1724     15     29    -57  A    C
ATOM   3635  CB  LYS A 640      25.762 -12.841   3.937  1.00 14.76           A    C
ANISOU 3635  CB  LYS A 640    1814   1870   1922     79    -19    -39  A    C
ATOM   3638  CG  LYS A 640      26.269 -12.150   2.705  1.00 18.43           A    C
ANISOU 3638  CG  LYS A 640    2373   2339   2290     30     24     47  A    C
ATOM   3641  CD  LYS A 640      27.669 -11.557   2.921  1.00 22.16           A    C
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ANISOU 3641  CD  LYS A 640     2652   2838   2927    -72    -22     25  A    C
ATOM   3644  CE  LYS A 640      27.703 -10.410   3.923  1.00 24.61      A    C
ANISOU 3644  CE  LYS A 640     3123   3082   3146     -3    -31    -54  A    C
ATOM   3647  NZ  LYS A 640      27.280  -9.091   3.342  1.00 26.76      A    N
ANISOU 3647  NZ  LYS A 640     3415   3270   3481     22    -90     42  A    N
ATOM   3651  C   LYS A 640      24.222 -14.495   4.969  1.00 13.21      A    C
ANISOU 3651  C   LYS A 640     1750   1627   1642     55    -17    -59  A    C
ATOM   3652  O   LYS A 640      25.003 -15.379   5.284  1.00 14.21      A    O
ANISOU 3652  O   LYS A 640     1849   1720   1830    113     74   -123  A    O
ATOM   3653  N   GLY A 641      23.165 -14.174   5.710  1.00 12.64      A    N
ANISOU 3653  N   GLY A 641     1659   1512   1631     61     25     -4  A    N
ATOM   3655  CA  GLY A 641      22.779 -14.925   6.891  1.00 12.25      A    C
ANISOU 3655  CA  GLY A 641     1573   1501   1581     78     62    -74  A    C
ATOM   3658  C   GLY A 641      23.279 -14.317   8.179  1.00 12.26      A    C
ANISOU 3658  C   GLY A 641     1571   1525   1560     69     52    -26  A    C
ATOM   3659  O   GLY A 641      23.066 -14.893   9.246  1.00 13.24      A    O
ANISOU 3659  O   GLY A 641     1826   1595   1610    105     87    -74  A    O
ATOM   3660  N   ASP A 642      23.948 -13.170   8.085  1.00 11.89      A    N
ANISOU 3660  N   ASP A 642     1482   1543   1492     77     61    -95  A    N
ATOM   3662  CA  ASP A 642      24.444 -12.472   9.264  1.00 11.79      A    C
ANISOU 3662  CA  ASP A 642     1506   1482   1490     57     16    -51  A    C
ATOM   3664  CB  ASP A 642      25.450 -11.384   8.862  1.00 13.17      A    C
ANISOU 3664  CB  ASP A 642     1673   1652   1677      5     -3    -34  A    C
ATOM   3667  CG  ASP A 642      26.755 -11.922   8.340  1.00 16.93      A    C
ANISOU 3667  CG  ASP A 642     2055   2221   2153     50     20    -29  A    C
ATOM   3668  OD1 ASP A 642      27.067 -13.113   8.550  1.00 19.65      A    O
ANISOU 3668  OD1 ASP A 642     2418   2245   2802    109     13   -157  A    O
ATOM   3669  OD2 ASP A 642      27.559 -11.174   7.734  1.00 21.95      A    O
ANISOU 3669  OD2 ASP A 642     2641   2883   2816   -148    157     28  A    O
ATOM   3670  C   ASP A 642      23.254 -11.811   9.997  1.00 10.88      A    C
ANISOU 3670  C   ASP A 642     1379   1386   1368     36    -19    -54  A    C
ATOM   3671  O   ASP A 642      22.269 -11.384   9.384  1.00  9.89      A    O
ANISOU 3671  O   ASP A 642     1325   1187   1245     48     91    -99  A    O
ATOM   3672  N   ARG A 643      23.394 -11.705  11.309  1.00 10.17      A    N
ANISOU 3672  N   ARG A 643     1299   1312   1253     40     49     32  A    N
ATOM   3674  CA  ARG A 643      22.358 -11.145  12.170  1.00 10.74      A    C
ANISOU 3674  CA  ARG A 643     1403   1320   1358     39     12     -7  A    C
ATOM   3676  CB  ARG A 643      21.507 -12.257  12.804  1.00 11.04      A    C
ANISOU 3676  CB  ARG A 643     1392   1433   1367     32     17     19  A    C
ATOM   3679  CG  ARG A 643      20.724 -13.122  11.814  1.00 11.65      A    C
ANISOU 3679  CG  ARG A 643     1613   1338   1475     24     66    -11  A    C
ATOM   3682  CD  ARG A 643      19.638 -12.359  11.087  1.00 11.09      A    C
ANISOU 3682  CD  ARG A 643     1367   1546   1298    -35     75    -80  A    C
ATOM   3685  NE  ARG A 643      18.829 -13.196  10.204  1.00 12.34      A    N
ANISOU 3685  NE  ARG A 643     1455   1520   1714   -103     55    -32  A    N
ATOM   3687  CZ  ARG A 643      19.073 -13.441   8.918  1.00 12.04      A    C
ANISOU 3687  CZ  ARG A 643     1477   1458   1639    -51     78      5  A    C
ATOM   3688  NH1 ARG A 643      20.134 -12.927   8.306  1.00  8.18      A    N
ANISOU 3688  NH1 ARG A 643     1163   1026    917     10     72   -183  A    N
ATOM   3691  NH2 ARG A 643      18.234 -14.212   8.225  1.00 12.82      A    N
ANISOU 3691  NH2 ARG A 643     1696   1600   1572     59     58   -141  A    N
ATOM   3694  C   ARG A 643      22.990 -10.277  13.248  1.00 10.07      A    C
ANISOU 3694  C   ARG A 643     1304   1257   1264     11     32     23  A    C
ATOM   3695  O   ARG A 643      24.202 -10.312  13.480  1.00 11.11      A    O
ANISOU 3695  O   ARG A 643     1409   1440   1370     50    -37    -52  A    O
ATOM   3696  N   LEU A 644      22.171  -9.452  13.881  1.00  9.23      A    N
ANISOU 3696  N   LEU A 644     1088   1167   1250     11      0     12  A    N
ATOM   3698  CA  LEU A 644      22.605  -8.720  15.057  1.00  8.97      A    C
ANISOU 3698  CA  LEU A 644     1120   1110   1178    -26     41     30  A    C
ATOM   3700  CB  LEU A 644      21.442  -7.941  15.659  1.00  8.90      A    C
ANISOU 3700  CB  LEU A 644     1134   1133   1111     16    -35    -40  A    C
ATOM   3703  CG  LEU A 644      20.872  -6.812  14.792  1.00  8.68      A    C
ANISOU 3703  CG  LEU A 644     1160    967   1168    -50     24      5  A    C
ATOM   3705  CD1 LEU A 644      19.472  -6.410  15.278  1.00  9.88      A    C
ANISOU 3705  CD1 LEU A 644     1287   1162   1305    -33    -26      4  A    C
ATOM   3709  CD2 LEU A 644      21.782  -5.605  14.760  1.00  9.21      A    C
ANISOU 3709  CD2 LEU A 644     1135   1211   1152   -138    -38     80  A    C
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ATOM   3713  C   LEU A 644      23.176  -9.701  16.080  1.00  8.86           A    C
ANISOU 3713  C   LEU A 644    1091   1091   1183    -28     32     36  A    C
ATOM   3714  O   LEU A 644      22.570 -10.754  16.337  1.00  9.64           A    O
ANISOU 3714  O   LEU A 644    1216   1033   1413   -109      4     33  A    O
ATOM   3715  N   PRO A 645      24.316  -9.380  16.685  1.00  9.03           A    N
ANISOU 3715  N   PRO A 645    1145   1108   1174    -66     26     19  A    N
ATOM   3716  CA  PRO A 645      24.919 -10.294  17.665  1.00  8.83           A    C
ANISOU 3716  CA  PRO A 645    1092   1090   1172     -9      2    -12  A    C
ATOM   3718  CB  PRO A 645      26.331  -9.729  17.832  1.00 10.39           A    C
ANISOU 3718  CB  PRO A 645    1214   1345   1387    -91    -17     34  A    C
ATOM   3721  CG  PRO A 645      26.141  -8.252  17.675  1.00 11.21           A    C
ANISOU 3721  CG  PRO A 645    1375   1399   1483   -173    -50     23  A    C
ATOM   3724  CD  PRO A 645      25.104  -8.133  16.539  1.00 10.07           A    C
ANISOU 3724  CD  PRO A 645    1273   1288   1263    -88     14    133  A    C
ATOM   3727  C   PRO A 645      24.188 -10.276  18.993  1.00  8.79           A    C
ANISOU 3727  C   PRO A 645    1117   1066   1155     10     29     33  A    C
ATOM   3728  O   PRO A 645      23.520  -9.313  19.322  1.00  9.49           A    O
ANISOU 3728  O   PRO A 645    1330   1031   1242    131     70    130  A    O
ATOM   3729  N   LYS A 646      24.381 -11.295  19.803  1.00  8.65           A    N
ANISOU 3729  N   LYS A 646    1172   1019   1096     14     48     25  A    N
ATOM   3731  CA  LYS A 646      23.756 -11.323  21.111  1.00  9.22           A    C
ANISOU 3731  CA  LYS A 646    1217   1096   1189     -5     49     15  A    C
ATOM   3733  CB  LYS A 646      24.026 -12.666  21.801  1.00 10.45           A    C
ANISOU 3733  CB  LYS A 646    1475   1215   1280    -32    -24     27  A    C
ATOM   3736  CG  LYS A 646      23.202 -12.745  23.076  1.00 12.24           A    C
ANISOU 3736  CG  LYS A 646    1631   1586   1431    -97     89    -12  A    C
ATOM   3739  CD  LYS A 646      23.314 -14.080  23.805  1.00 15.66           A    C
ANISOU 3739  CD  LYS A 646    2158   1847   1945    -24     -7     72  A    C
ATOM   3742  CE  LYS A 646      24.596 -14.159  24.612  1.00 16.74           A    C
ANISOU 3742  CE  LYS A 646    2145   2027   2189     -7    -35     75  A    C
ATOM   3745  NZ  LYS A 646      24.740 -13.087  25.672  1.00 16.74           A    N
ANISOU 3745  NZ  LYS A 646    2122   2081   2158     13    -57     29  A    N
ATOM   3749  C   LYS A 646      24.268 -10.174  21.975  1.00  8.79           A    C
ANISOU 3749  C   LYS A 646    1117   1147   1072    -37     65     17  A    C
ATOM   3750  O   LYS A 646      25.483 -10.056  22.190  1.00  9.36           A    O
ANISOU 3750  O   LYS A 646    1116   1274   1166    -99     16   -103  A    O
ATOM   3751  N   PRO A 647      23.380  -9.325  22.495  1.00  9.12           A    N
ANISOU 3751  N   PRO A 647    1134   1137   1192    -24      5     24  A    N
ATOM   3752  CA  PRO A 647      23.816  -8.335  23.492  1.00  9.77           A    C
ANISOU 3752  CA  PRO A 647    1255   1202   1252    -27     45      9  A    C
ATOM   3754  CB  PRO A 647      22.517  -7.593  23.838  1.00  9.88           A    C
ANISOU 3754  CB  PRO A 647    1247   1242   1264    -32     58     17  A    C
ATOM   3757  CG  PRO A 647      21.672  -7.760  22.648  1.00 10.13           A    C
ANISOU 3757  CG  PRO A 647    1322   1330   1195     12     92    -62  A    C
ATOM   3760  CD  PRO A 647      21.944  -9.159  22.159  1.00  9.19           A    C
ANISOU 3760  CD  PRO A 647    1102   1182   1208    -66     62    -25  A    C
ATOM   3763  C   PRO A 647      24.421  -9.023  24.713  1.00  9.70           A    C
ANISOU 3763  C   PRO A 647    1264   1200   1221    -18     57    -31  A    C
ATOM   3764  O   PRO A 647      23.980 -10.129  25.069  1.00  9.56           A    O
ANISOU 3764  O   PRO A 647    1272   1232   1126     61     47    137  A    O
ATOM   3765  N   ASP A 648      25.412  -8.395  25.331  1.00 10.93           A    N
ANISOU 3765  N   ASP A 648    1409   1374   1367    -15    -47     30  A    N
ATOM   3767  CA  ASP A 648      26.106  -9.004  26.465  1.00 12.88           A    C
ANISOU 3767  CA  ASP A 648    1616   1657   1621    -20    -20     55  A    C
ATOM   3769  CB  ASP A 648      27.097  -8.015  27.064  1.00 14.05           A    C
ANISOU 3769  CB  ASP A 648    1815   1786   1737    -47    -27     51  A    C
ATOM   3772  CG  ASP A 648      28.032  -8.674  28.039  1.00 16.34           A    C
ANISOU 3772  CG  ASP A 648    1947   2173   2089     -3    -79    120  A    C
ATOM   3773  OD1 ASP A 648      28.724  -9.649  27.667  1.00 18.87           A    O
ANISOU 3773  OD1 ASP A 648    2317   2422   2429     23    -40     85  A    O
ATOM   3774  OD2 ASP A 648      28.101  -8.282  29.203  1.00 22.16           A    O
ANISOU 3774  OD2 ASP A 648    2868   3064   2484    -75    -60    -50  A    O
ATOM   3775  C   ASP A 648      25.171  -9.560  27.553  1.00 13.03           A    C
ANISOU 3775  C   ASP A 648    1705   1634   1611     -6     -8     50  A    C
ATOM   3776  O   ASP A 648      25.364 -10.693  28.018  1.00 13.83           A    O
ANISOU 3776  O   ASP A 648    1774   1758   1721      5    -70    164  A    O
ATOM   3777  N   LEU A 649      24.149  -8.786  27.915  1.00 12.78           A    N
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ANISOU 3777  N   LEU A 649     1646   1649   1561    -39     12     53  A    N
ATOM   3779  CA  LEU A 649      23.264  -9.140  29.021  1.00 13.30           A    C
ANISOU 3779  CA  LEU A 649     1688   1718   1644    -23     31     30  A    C
ATOM   3781  CB  LEU A 649      22.863  -7.892  29.802  1.00 14.42           A    C
ANISOU 3781  CB  LEU A 649     1918   1812   1746    -27     91     48  A    C
ATOM   3784  CG  LEU A 649      24.018  -7.251  30.578  1.00 17.26           A    C
ANISOU 3784  CG  LEU A 649     2139   2165   2252    -76    -15     36  A    C
ATOM   3786  CD1 LEU A 649      23.487  -6.172  31.477  1.00 18.90           A    C
ANISOU 3786  CD1 LEU A 649     2457   2412   2310    -10     64    -22  A    C
ATOM   3790  CD2 LEU A 649      24.837  -8.239  31.400  1.00 18.74           A    C
ANISOU 3790  CD2 LEU A 649     2434   2340   2344    -27    -47     29  A    C
ATOM   3794  C   LEU A 649      22.023  -9.898  28.582  1.00 12.89           A    C
ANISOU 3794  C   LEU A 649     1674   1674   1549    -40     53     11  A    C
ATOM   3795  O   LEU A 649      21.196 -10.263  29.410  1.00 14.26           A    O
ANISOU 3795  O   LEU A 649     1827   1867   1723   -137    203    -12  A    O
ATOM   3796  N   CYS A 650      21.901 -10.178  27.293  1.00 11.79           A    N
ANISOU 3796  N   CYS A 650     1537   1537   1405    -36     72     38  A    N
ATOM   3798  CA  CYS A 650      20.795 -10.967  26.806  1.00 11.54           A    C
ANISOU 3798  CA  CYS A 650     1456   1487   1441     45     32     20  A    C
ATOM   3800  CB  CYS A 650      20.692 -10.790  25.289  1.00 11.36           A    C
ANISOU 3800  CB  CYS A 650     1450   1460   1405     68     18      0  A    C
ATOM   3803  SG  CYS A 650      19.303 -11.660  24.541  1.00 11.66           A    S
ANISOU 3803  SG  CYS A 650     1267   1459   1704    -18     63    226  A    S
ATOM   3804  C   CYS A 650      20.955 -12.455  27.154  1.00 12.36           A    C
ANISOU 3804  C   CYS A 650     1592   1586   1518     62     27     57  A    C
ATOM   3805  O   CYS A 650      21.955 -13.058  26.782  1.00 12.76           A    O
ANISOU 3805  O   CYS A 650     1653   1586   1608     93     60     78  A    O
ATOM   3806  N   PRO A 651      19.971 -13.037  27.854  1.00 12.87           A    N
ANISOU 3806  N   PRO A 651     1684   1537   1669     12     13     82  A    N
ATOM   3807  CA  PRO A 651      19.951 -14.479  28.113  1.00 13.18           A    C
ANISOU 3807  CA  PRO A 651     1681   1611   1713    -19    -27     10  A    C
ATOM   3809  CB  PRO A 651      18.565 -14.681  28.747  1.00 13.38           A    C
ANISOU 3809  CB  PRO A 651     1800   1640   1643    -86     60     25  A    C
ATOM   3812  CG  PRO A 651      18.243 -13.418  29.381  1.00 14.43           A    C
ANISOU 3812  CG  PRO A 651     1817   1781   1884    -21     21     80  A    C
ATOM   3815  CD  PRO A 651      18.812 -12.370  28.476  1.00 13.39           A    C
ANISOU 3815  CD  PRO A 651     1734   1739   1611    -46     38     90  A    C
ATOM   3818  C   PRO A 651      20.038 -15.273  26.797  1.00 12.61           A    C
ANISOU 3818  C   PRO A 651     1610   1521   1657    -26    -50     21  A    C
ATOM   3819  O   PRO A 651      19.355 -14.918  25.853  1.00 11.79           A    O
ANISOU 3819  O   PRO A 651     1532   1282   1664     -5   -135    223  A    O
ATOM   3820  N   PRO A 652      20.867 -16.303  26.703  1.00 13.43           A    N
ANISOU 3820  N   PRO A 652     1665   1683   1753     46   -124     69  A    N
ATOM   3821  CA  PRO A 652      20.896 -17.142  25.503  1.00 13.03           A    C
ANISOU 3821  CA  PRO A 652     1648   1583   1718     24    -79     79  A    C
ATOM   3823  CB  PRO A 652      21.794 -18.317  25.917  1.00 14.64           A    C
ANISOU 3823  CB  PRO A 652     1883   1729   1950     48    -76     45  A    C
ATOM   3826  CG  PRO A 652      22.676 -17.726  26.935  1.00 13.89           A    C
ANISOU 3826  CG  PRO A 652     1659   1752   1866     84   -100    111  A    C
ATOM   3829  CD  PRO A 652      21.904 -16.682  27.680  1.00 14.14           A    C
ANISOU 3829  CD  PRO A 652     1710   1804   1856     15   -163     52  A    C
ATOM   3832  C   PRO A 652      19.513 -17.594  24.987  1.00 12.68           A    C
ANISOU 3832  C   PRO A 652     1619   1532   1667     26     -4     52  A    C
ATOM   3833  O   PRO A 652      19.282 -17.552  23.788  1.00 11.79           A    O
ANISOU 3833  O   PRO A 652     1536   1290   1652     46    -71    124  A    O
ATOM   3834  N   VAL A 653      18.613 -17.983  25.878  1.00 12.27           A    N
ANISOU 3834  N   VAL A 653     1597   1420   1644      9    -14     62  A    N
ATOM   3836  CA  VAL A 653      17.281 -18.416  25.481  1.00 12.50           A    C
ANISOU 3836  CA  VAL A 653     1605   1486   1655     26     -5     34  A    C
ATOM   3838  CB  VAL A 653      16.469 -18.936  26.708  1.00 13.38           A    C
ANISOU 3838  CB  VAL A 653     1764   1651   1667     29     16     69  A    C
ATOM   3840  CG1 VAL A 653      16.253 -17.882  27.778  1.00 15.20           A    C
ANISOU 3840  CG1 VAL A 653     2033   1871   1871    -10    -22    -18  A    C
ATOM   3844  CG2 VAL A 653      15.128 -19.484  26.305  1.00 14.80           A    C
ANISOU 3844  CG2 VAL A 653     1877   1758   1985     -6    -46     -2  A    C
ATOM   3848  C   VAL A 653      16.529 -17.293  24.764  1.00 11.55           A    C
ANISOU 3848  C   VAL A 653     1522   1370   1497     -6     12     35  A    C
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ATOM   3849  O   VAL A 653      15.803 -17.533  23.784  1.00 11.72           A    O
ANISOU 3849  O   VAL A 653    1487   1334   1631     25     37     28  A    O
ATOM   3850  N   LEU A 654      16.725 -16.061  25.234  1.00 10.59           A    N
ANISOU 3850  N   LEU A 654    1369   1240   1414      3     -7     91  A    N
ATOM   3852  CA  LEU A 654      16.111 -14.926  24.553  1.00 10.31           A    C
ANISOU 3852  CA  LEU A 654    1279   1271   1366     29    -58     80  A    C
ATOM   3854  CB  LEU A 654      16.141 -13.704  25.461  1.00 10.74           A    C
ANISOU 3854  CB  LEU A 654    1411   1293   1375     61     37     61  A    C
ATOM   3857  CG  LEU A 654      15.488 -12.434  24.897  1.00 10.90           A    C
ANISOU 3857  CG  LEU A 654    1365   1352   1424     80     28     54  A    C
ATOM   3859  CD1 LEU A 654      14.034 -12.661  24.526  1.00 12.25           A    C
ANISOU 3859  CD1 LEU A 654    1549   1513   1593    -63     62     49  A    C
ATOM   3863  CD2 LEU A 654      15.658 -11.283  25.870  1.00 13.59           A    C
ANISOU 3863  CD2 LEU A 654    1829   1668   1667    -25     74    -61  A    C
ATOM   3867  C   LEU A 654      16.748 -14.626  23.194  1.00  9.80           A    C
ANISOU 3867  C   LEU A 654    1217   1122   1383     38    -40     18  A    C
ATOM   3868  O   LEU A 654      16.050 -14.304  22.234  1.00 10.34           A    O
ANISOU 3868  O   LEU A 654    1264   1232   1432     20    -54     53  A    O
ATOM   3869  N   TYR A 655      18.064 -14.745  23.086  1.00  9.87           A    N
ANISOU 3869  N   TYR A 655    1236   1163   1351     18     18    117  A    N
ATOM   3871  CA  TYR A 655      18.691 -14.605  21.780  1.00  9.35           A    C
ANISOU 3871  CA  TYR A 655    1195   1144   1210     12      0    -29  A    C
ATOM   3873  CB  TYR A 655      20.203 -14.628  21.896  1.00  8.79           A    C
ANISOU 3873  CB  TYR A 655    1147   1073   1118     30      0     44  A    C
ATOM   3876  CG  TYR A 655      20.876 -14.257  20.615  1.00  9.30           A    C
ANISOU 3876  CG  TYR A 655    1057   1198   1277    -17     60    125  A    C
ATOM   3877  CD1 TYR A 655      20.735 -12.989  20.095  1.00  9.13           A    C
ANISOU 3877  CD1 TYR A 655    997   1062   1409     51    -33     65  A    C
ATOM   3879  CE1 TYR A 655      21.335 -12.634  18.891  1.00  9.04           A    C
ANISOU 3879  CE1 TYR A 655    1110   1023   1301    -81     -9    -42  A    C
ATOM   3881  CZ  TYR A 655      22.097 -13.558  18.203  1.00 10.17           A    C
ANISOU 3881  CZ  TYR A 655    1228   1269   1366    -32     85     21  A    C
ATOM   3882  OH  TYR A 655      22.675 -13.209  17.020  1.00 12.04           A    O
ANISOU 3882  OH  TYR A 655    1460   1598   1517    -29    248    -27  A    O
ATOM   3884  CE2 TYR A 655      22.238 -14.845  18.695  1.00 10.02           A    C
ANISOU 3884  CE2 TYR A 655    1312   1224   1271     95    102    -12  A    C
ATOM   3886  CD2 TYR A 655      21.635 -15.186  19.902  1.00  9.51           A    C
ANISOU 3886  CD2 TYR A 655    1169   1128   1316     95     36    173  A    C
ATOM   3888  C   TYR A 655      18.194 -15.670  20.789  1.00  9.65           A    C
ANISOU 3888  C   TYR A 655    1216   1137   1313     37      0    -15  A    C
ATOM   3889  O   TYR A 655      17.978 -15.375  19.643  1.00 10.05           A    O
ANISOU 3889  O   TYR A 655    1207   1195   1415     30     58    -67  A    O
ATOM   3890  N   THR A 656      17.986 -16.896  21.245  1.00 10.25           A    N
ANISOU 3890  N   THR A 656    1328   1203   1360     11     -7    -43  A    N
ATOM   3892  CA  THR A 656      17.441 -17.911  20.338  1.00 11.61           A    C
ANISOU 3892  CA  THR A 656    1548   1345   1516     -3    -48     -8  A    C
ATOM   3894  CB  THR A 656      17.341 -19.223  21.104  1.00 12.32           A    C
ANISOU 3894  CB  THR A 656    1614   1469   1597    -40    -43     39  A    C
ATOM   3896  OG1 THR A 656      18.672 -19.666  21.427  1.00 14.62           A    O
ANISOU 3896  OG1 THR A 656    1925   1540   2089    151   -187     79  A    O
ATOM   3898  CG2 THR A 656      16.743 -20.321  20.246  1.00 13.85           A    C
ANISOU 3898  CG2 THR A 656    1924   1485   1852     17     13    -75  A    C
ATOM   3902  C   THR A 656      16.068 -17.470  19.808  1.00 11.48           A    C
ANISOU 3902  C   THR A 656    1500   1366   1493    -78     13     63  A    C
ATOM   3903  O   THR A 656      15.760 -17.625  18.625  1.00 12.21           A    O
ANISOU 3903  O   THR A 656    1610   1445   1582    -17    -80     64  A    O
ATOM   3904  N   LEU A 657      15.256 -16.904  20.678  1.00 11.37           A    N
ANISOU 3904  N   LEU A 657    1456   1359   1504    -48    -71     71  A    N
ATOM   3906  CA  LEU A 657      13.967 -16.388  20.270  1.00 11.26           A    C
ANISOU 3906  CA  LEU A 657    1370   1402   1504    -10    -47     46  A    C
ATOM   3908  CB  LEU A 657      13.194 -15.883  21.490  1.00 12.25           A    C
ANISOU 3908  CB  LEU A 657    1537   1510   1606     36    -40    -46  A    C
ATOM   3911  CG  LEU A 657      11.691 -15.721  21.318  1.00 15.01           A    C
ANISOU 3911  CG  LEU A 657    1807   1933   1962    -50     14     68  A    C
ATOM   3913  CD1 LEU A 657      11.055 -17.063  21.001  1.00 16.78           A    C
ANISOU 3913  CD1 LEU A 657    2124   2040   2210   -138     61   -141  A    C
ATOM   3917  CD2 LEU A 657      11.099 -15.144  22.592  1.00 16.43           A    C
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ANISOU 3917  CD2 LEU A 657     2124   1949   2167     48     52   -153  A    C
ATOM   3921  C   LEU A 657      14.107 -15.291  19.228  1.00 10.50        A    C
ANISOU 3921  C   LEU A 657     1237   1328   1424    -25    -59      9  A    C
ATOM   3922  O   LEU A 657      13.389 -15.290  18.221  1.00 11.31        A    O
ANISOU 3922  O   LEU A 657     1323   1397   1575    140   -163     13  A    O
ATOM   3923  N   MET A 658      15.016 -14.348  19.466  1.00  9.64        A    N
ANISOU 3923  N   MET A 658     1161   1248   1252     16    -70     37  A    N
ATOM   3925  CA  MET A 658      15.275 -13.301  18.493  1.00  9.56        A    C
ANISOU 3925  CA  MET A 658     1159   1209   1264     51    -40     67  A    C
ATOM   3927  CB  MET A 658      16.419 -12.415  18.942  1.00  9.94        A    C
ANISOU 3927  CB  MET A 658     1247   1282   1248     21    -29     47  A    C
ATOM   3930  CG  MET A 658      16.115 -11.495  20.092  1.00 11.63        A    C
ANISOU 3930  CG  MET A 658     1400   1521   1497     82    -67   -126  A    C
ATOM   3933  SD  MET A 658      17.671 -10.658  20.635  1.00 15.26        A    S
ANISOU 3933  SD  MET A 658     1778   1684   2337    162   -495   -211  A    S
ATOM   3934  CE  MET A 658      17.105  -9.738  22.088  1.00 15.81        A    C
ANISOU 3934  CE  MET A 658     1841   2062   2103    -23     31     40  A    C
ATOM   3938  C   MET A 658      15.638 -13.894  17.136  1.00  9.77        A    C
ANISOU 3938  C   MET A 658     1215   1234   1261      3    -38     51  A    C
ATOM   3939  O   MET A 658      15.151 -13.440  16.106  1.00 10.18        A    O
ANISOU 3939  O   MET A 658     1308   1171   1389    -26   -102     54  A    O
ATOM   3940  N   THR A 659      16.505 -14.908  17.131  1.00 10.09        A    N
ANISOU 3940  N   THR A 659     1266   1213   1351      3    -82     69  A    N
ATOM   3942  CA  THR A 659      17.000 -15.494  15.881  1.00 11.51        A    C
ANISOU 3942  CA  THR A 659     1419   1436   1516     37      1     33  A    C
ATOM   3944  CB  THR A 659      18.166 -16.476  16.089  1.00 13.24        A    C
ANISOU 3944  CB  THR A 659     1513   1728   1789     80    -18      3  A    C
ATOM   3946  OG1 THR A 659      17.735 -17.581  16.856  1.00 17.70        A    O
ANISOU 3946  OG1 THR A 659     2269   2217   2237    110     38    191  A    O
ATOM   3948  CG2 THR A 659      19.279 -15.883  16.898  1.00 12.51        A    C
ANISOU 3948  CG2 THR A 659     1570   1593   1589    148     10    -58  A    C
ATOM   3952  C   THR A 659      15.882 -16.137  15.081  1.00 10.45        A    C
ANISOU 3952  C   THR A 659     1414   1209   1347     38     16    -37  A    C
ATOM   3953  O   THR A 659      15.909 -16.094  13.858  1.00 10.83        A    O
ANISOU 3953  O   THR A 659     1385   1405   1322     80     -1      3  A    O
ATOM   3954  N   ARG A 660      14.900 -16.721  15.777  1.00 10.63        A    N
ANISOU 3954  N   ARG A 660     1337   1349   1351     57     20    -64  A    N
ATOM   3956  CA  ARG A 660      13.700 -17.276  15.145  1.00 11.35        A    C
ANISOU 3956  CA  ARG A 660     1414   1422   1475    -10     11    -18  A    C
ATOM   3958  CB  ARG A 660      12.851 -18.042  16.161  1.00 12.55        A    C
ANISOU 3958  CB  ARG A 660     1518   1653   1596    -43    -37      2  A    C
ATOM   3961  CG  ARG A 660      13.473 -19.353  16.555  1.00 15.60        A    C
ANISOU 3961  CG  ARG A 660     1962   1865   2097    -18    -82     44  A    C
ATOM   3964  CD  ARG A 660      12.801 -19.997  17.728  1.00 19.96        A    C
ANISOU 3964  CD  ARG A 660     2560   2590   2432     17     58     55  A    C
ATOM   3967  NE  ARG A 660      11.470 -20.429  17.337  1.00 22.64        A    N
ANISOU 3967  NE  ARG A 660     2742   2885   2975   -134     11     88  A    N
ATOM   3969  CZ  ARG A 660      10.390 -20.450  18.129  1.00 24.17        A    C
ANISOU 3969  CZ  ARG A 660     2979   3153   3050      8     71     -6  A    C
ATOM   3970  NH1 ARG A 660      10.448 -20.106  19.423  1.00 23.56        A    N
ANISOU 3970  NH1 ARG A 660     2853   2985   3111    -35     23    -91  A    N
ATOM   3973  NH2 ARG A 660       9.240 -20.866  17.608  1.00 25.14        A    N
ANISOU 3973  NH2 ARG A 660     3066   3291   3193    -70    -15    -17  A    N
ATOM   3976  C   ARG A 660      12.861 -16.187  14.479  1.00 10.39        A    C
ANISOU 3976  C   ARG A 660     1306   1255   1386    -38      6    -32  A    C
ATOM   3977  O   ARG A 660      12.333 -16.373  13.387  1.00 11.12        A    O
ANISOU 3977  O   ARG A 660     1386   1295   1540    -51      3   -122  A    O
ATOM   3978  N   CYS A 661      12.743 -15.040  15.145  1.00  9.59        A    N
ANISOU 3978  N   CYS A 661     1241   1145   1255    -52     45    -22  A    N
ATOM   3980  CA  CYS A 661      12.046 -13.902  14.564  1.00  9.30        A    C
ANISOU 3980  CA  CYS A 661     1063   1228   1241    -46     23     34  A    C
ATOM   3982  CB  CYS A 661      11.912 -12.785  15.587  1.00  9.52        A    C
ANISOU 3982  CB  CYS A 661     1113   1160   1343   -110    -33     36  A    C
ATOM   3985  SG  CYS A 661      10.905 -13.173  17.035  1.00 10.38        A    S
ANISOU 3985  SG  CYS A 661     1174   1273   1497     -2     34      0  A    S
ATOM   3986  C   CYS A 661      12.762 -13.337  13.350  1.00  9.87        A    C
ANISOU 3986  C   CYS A 661     1220   1284   1246    -12    -15     13  A    C
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ATOM   3987  O   CYS A 661      12.141 -12.648  12.551  1.00 10.25           A    O
ANISOU 3987  O   CYS A 661       989   1459   1447     80    -13     74  A    O
ATOM   3988  N   TRP A 662      14.069 -13.607  13.254  1.00  9.56           A    N
ANISOU 3988  N   TRP A 662      1119   1241   1270     42     44     49  A    N
ATOM   3990  CA  TRP A 662      14.878 -13.186  12.101  1.00  8.71           A    C
ANISOU 3990  CA  TRP A 662      1143   1052   1114     28    -16    -23  A    C
ATOM   3992  CB  TRP A 662      16.211 -12.595  12.536  1.00  8.84           A    C
ANISOU 3992  CB  TRP A 662      1144   1066   1147    -38     68     10  A    C
ATOM   3995  CG  TRP A 662      16.102 -11.404  13.435  1.00  9.51           A    C
ANISOU 3995  CG  TRP A 662      1168   1100   1346     20    -13    -20  A    C
ATOM   3996  CD1 TRP A 662      15.154 -10.420  13.419  1.00  9.22           A    C
ANISOU 3996  CD1 TRP A 662      1067   1175   1259    -60     36     36  A    C
ATOM   3998  NE1 TRP A 662      15.420  -9.495  14.399  1.00  9.46           A    N
ANISOU 3998  NE1 TRP A 662      1068   1133   1392    115     20    -55  A    N
ATOM   4000  CE2 TRP A 662      16.518  -9.904  15.105  1.00  8.11           A    C
ANISOU 4000  CE2 TRP A 662      1012    881   1187     12     28     37  A    C
ATOM   4001  CD2 TRP A 662      16.975 -11.091  14.516  1.00  7.35           A    C
ANISOU 4001  CD2 TRP A 662      1014    780    995   -118    148     24  A    C
ATOM   4002  CE3 TRP A 662      18.111 -11.697  15.051  1.00  8.68           A    C
ANISOU 4002  CE3 TRP A 662      1199    926   1172    -98     39    132  A    C
ATOM   4004  CZ3 TRP A 662      18.733 -11.119  16.123  1.00  9.60           A    C
ANISOU 4004  CZ3 TRP A 662      1434   1045   1168    -56     51     88  A    C
ATOM   4006  CH2 TRP A 662      18.273  -9.927  16.659  1.00  9.22           A    C
ANISOU 4006  CH2 TRP A 662      1177   1161   1164      7    -14    -46  A    C
ATOM   4008  CZ2 TRP A 662      17.169  -9.317  16.174  1.00  7.78           A    C
ANISOU 4008  CZ2 TRP A 662      1169    709   1076    -72     94    138  A    C
ATOM   4010  C   TRP A 662      15.091 -14.293  11.055  1.00  9.58           A    C
ANISOU 4010  C   TRP A 662      1267   1208   1161     17     19    -24  A    C
ATOM   4011  O   TRP A 662      16.022 -14.238  10.263  1.00 11.04           A    O
ANISOU 4011  O   TRP A 662      1307   1505   1380    -17    -57    -62  A    O
ATOM   4012  N   ASP A 663      14.165 -15.243  11.005  1.00 10.56           A    N
ANISOU 4012  N   ASP A 663      1377   1332   1301     32    -22    -57  A    N
ATOM   4014  CA  ASP A 663      14.176 -16.193   9.910  1.00 11.21           A    C
ANISOU 4014  CA  ASP A 663      1435   1385   1438     60     73    -84  A    C
ATOM   4016  CB  ASP A 663      13.095 -17.242  10.080  1.00 11.68           A    C
ANISOU 4016  CB  ASP A 663      1559   1379   1497      6     29    -34  A    C
ATOM   4019  CG  ASP A 663      13.384 -18.471   9.271  1.00 15.73           A    C
ANISOU 4019  CG  ASP A 663      2147   1777   2052     27     92   -166  A    C
ATOM   4020  OD1 ASP A 663      13.415 -18.374   8.027  1.00 19.86           A    O
ANISOU 4020  OD1 ASP A 663      2651   2427   2466    -53     98    162  A    O
ATOM   4021  OD2 ASP A 663      13.604 -19.579   9.797  1.00 20.97           A    O
ANISOU 4021  OD2 ASP A 663      2867   2382   2717    156    -18    183  A    O
ATOM   4022  C   ASP A 663      13.942 -15.414   8.615  1.00 11.04           A    C
ANISOU 4022  C   ASP A 663      1362   1405   1425     18     64    -36  A    C
ATOM   4023  O   ASP A 663      13.080 -14.535   8.551  1.00 10.98           A    O
ANISOU 4023  O   ASP A 663      1368   1406   1396    145    173   -154  A    O
ATOM   4024  N   TYR A 664      14.746 -15.668   7.595  1.00 10.94           A    N
ANISOU 4024  N   TYR A 664      1408   1386   1359     72     94   -108  A    N
ATOM   4026  CA  TYR A 664      14.585 -14.938   6.347  1.00 10.95           A    C
ANISOU 4026  CA  TYR A 664      1347   1436   1378     45     95    -37  A    C
ATOM   4028  CB  TYR A 664      15.646 -15.360   5.297  1.00 11.18           A    C
ANISOU 4028  CB  TYR A 664      1325   1543   1380    139     95   -100  A    C
ATOM   4031  CG  TYR A 664      15.836 -14.325   4.216  1.00 11.90           A    C
ANISOU 4031  CG  TYR A 664      1334   1598   1588    161    177    -86  A    C
ATOM   4032  CD1 TYR A 664      16.755 -13.283   4.376  1.00 14.52           A    C
ANISOU 4032  CD1 TYR A 664      1791   1876   1851    -14    159     37  A    C
ATOM   4034  CE1 TYR A 664      16.919 -12.312   3.387  1.00 15.63           A    C
ANISOU 4034  CE1 TYR A 664      1931   2039   1966     46    150     57  A    C
ATOM   4036  CZ  TYR A 664      16.155 -12.365   2.254  1.00 16.72           A    C
ANISOU 4036  CZ  TYR A 664      2101   2227   2025     63    130      5  A    C
ATOM   4037  OH  TYR A 664      16.340 -11.393   1.280  1.00 21.10           A    O
ANISOU 4037  OH  TYR A 664      2890   2467   2659     97    209    250  A    O
ATOM   4039  CE2 TYR A 664      15.244 -13.379   2.067  1.00 16.91           A    C
ANISOU 4039  CE2 TYR A 664      2151   2226   2049     94     44     34  A    C
ATOM   4041  CD2 TYR A 664      15.081 -14.355   3.046  1.00 15.74           A    C
ANISOU 4041  CD2 TYR A 664      1903   2090   1985     87    100    -38  A    C
ATOM   4043  C   TYR A 664      13.184 -15.126   5.764  1.00 11.55           A    C
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ANISOU 4043  C   TYR A 664     1432   1503   1452     45     72    -31  A    C
ATOM   4044  O   TYR A 664      12.633 -14.198   5.200  1.00 11.95       A    O
ANISOU 4044  O   TYR A 664     1366   1631   1543     58     76    -43  A    O
ATOM   4045  N   ASP A 665      12.641 -16.335   5.884  1.00 12.57       A    N
ANISOU 4045  N   ASP A 665     1548   1628   1600    -25     20    -86  A    N
ATOM   4047  CA  ASP A 665      11.298 -16.641   5.384  1.00 13.87       A    C
ANISOU 4047  CA  ASP A 665     1720   1757   1792    -25     16    -53  A    C
ATOM   4049  CB  ASP A 665      11.180 -18.149   5.120  1.00 15.39       A    C
ANISOU 4049  CB  ASP A 665     1989   1856   2003    -59     24    -51  A    C
ATOM   4052  CG  ASP A 665       9.937 -18.509   4.315  1.00 18.03       A    C
ANISOU 4052  CG  ASP A 665     2245   2238   2366    -93    -84    -45  A    C
ATOM   4053  OD1 ASP A 665       8.939 -17.743   4.326  1.00 19.13       A    O
ANISOU 4053  OD1 ASP A 665     2399   2438   2429    -66     91   -259  A    O
ATOM   4054  OD2 ASP A 665       9.884 -19.544   3.604  1.00 21.95       A    O
ANISOU 4054  OD2 ASP A 665     2938   2574   2828    -76    117   -313  A    O
ATOM   4055  C   ASP A 665      10.245 -16.208   6.398  1.00 13.43       A    C
ANISOU 4055  C   ASP A 665     1647   1716   1739    -63     -3    -50  A    C
ATOM   4056  O   ASP A 665      10.177 -16.799   7.466  1.00 13.05       A    O
ANISOU 4056  O   ASP A 665     1623   1633   1700    -89    135   -165  A    O
ATOM   4057  N   PRO A 666       9.415 -15.220   6.065  1.00 13.58       A    N
ANISOU 4057  N   PRO A 666     1661   1726   1773    -70      2    -67  A    N
ATOM   4058  CA  PRO A 666       8.384 -14.749   7.002  1.00 14.08       A    C
ANISOU 4058  CA  PRO A 666     1785   1800   1765    -58      7    -86  A    C
ATOM   4060  CB  PRO A 666       7.630 -13.674   6.206  1.00 14.61       A    C
ANISOU 4060  CB  PRO A 666     1813   1886   1849    -23     40    -36  A    C
ATOM   4063  CG  PRO A 666       8.031 -13.821   4.807  1.00 14.68       A    C
ANISOU 4063  CG  PRO A 666     1960   1798   1818     69     -5      9  A    C
ATOM   4066  CD  PRO A 666       9.358 -14.493   4.784  1.00 13.93       A    C
ANISOU 4066  CD  PRO A 666     1622   1871   1800    -95     29    -41  A    C
ATOM   4069  C   PRO A 666       7.444 -15.841   7.477  1.00 14.93       A    C
ANISOU 4069  C   PRO A 666     1843   1956   1872    -87     64    -64  A    C
ATOM   4070  O   PRO A 666       6.998 -15.834   8.615  1.00 13.71       A    O
ANISOU 4070  O   PRO A 666     1765   1733   1708   -155    120   -111  A    O
ATOM   4071  N   SER A 667       7.168 -16.808   6.611  1.00 15.82       A    N
ANISOU 4071  N   SER A 667     2055   2031   1924   -109     69   -104  A    N
ATOM   4073  CA  SER A 667       6.258 -17.902   6.962  1.00 17.09       A    C
ANISOU 4073  CA  SER A 667     2157   2139   2197    -69     67    -29  A    C
ATOM   4075  CB  SER A 667       5.990 -18.807   5.745  1.00 17.46       A    C
ANISOU 4075  CB  SER A 667     2184   2259   2190   -132     -2    -12  A    C
ATOM   4078  OG  SER A 667       5.326 -18.081   4.731  1.00 21.69       A    O
ANISOU 4078  OG  SER A 667     2671   2769   2801    -64    -20    101  A    O
ATOM   4080  C   SER A 667       6.758 -18.748   8.116  1.00 16.80       A    C
ANISOU 4080  C   SER A 667     2118   2078   2185    -36     57    -37  A    C
ATOM   4081  O   SER A 667       5.958 -19.438   8.742  1.00 18.68       A    O
ANISOU 4081  O   SER A 667     2284   2327   2485   -104    145    -21  A    O
ATOM   4082  N   ASP A 668       8.066 -18.697   8.405  1.00 16.50       A    N
ANISOU 4082  N   ASP A 668     2110   2001   2156    -22     90    -75  A    N
ATOM   4084  CA  ASP A 668       8.689 -19.497   9.442  1.00 16.07       A    C
ANISOU 4084  CA  ASP A 668     2049   1985   2071    -15     71    -56  A    C
ATOM   4086  CB  ASP A 668      10.047 -20.026   8.963  1.00 17.36       A    C
ANISOU 4086  CB  ASP A 668     2171   2170   2254     -5    107    -18  A    C
ATOM   4089  CG  ASP A 668       9.928 -20.986   7.786  1.00 20.84       A    C
ANISOU 4089  CG  ASP A 668     2672   2615   2630    -11     27   -166  A    C
ATOM   4090  OD1 ASP A 668       8.843 -21.546   7.549  1.00 23.33       A    O
ANISOU 4090  OD1 ASP A 668     2944   2843   3076    -59     43   -184  A    O
ATOM   4091  OD2 ASP A 668      10.891 -21.222   7.043  1.00 23.92       A    O
ANISOU 4091  OD2 ASP A 668     3031   3104   2953     55    199   -250  A    O
ATOM   4092  C   ASP A 668       8.917 -18.758  10.749  1.00 14.67       A    C
ANISOU 4092  C   ASP A 668     1864   1792   1914    -26     79      5  A    C
ATOM   4093  O   ASP A 668       9.392 -19.325  11.728  1.00 15.36       A    O
ANISOU 4093  O   ASP A 668     2059   1636   2140     56    125     55  A    O
ATOM   4094  N   ARG A 669       8.601 -17.477  10.771  1.00 12.20       A    N
ANISOU 4094  N   ARG A 669     1572   1520   1541     -8    130    -27  A    N
ATOM   4096  CA  ARG A 669       8.714 -16.724  12.017  1.00 11.14       A    C
ANISOU 4096  CA  ARG A 669     1360   1425   1445    -26     65    -12  A    C
ATOM   4098  CB  ARG A 669       8.675 -15.232  11.709  1.00 10.46       A    C
ANISOU 4098  CB  ARG A 669     1219   1353   1401    -24    104     -3  A    C
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ATOM   4101  CG  ARG A 669       9.864 -14.751  10.904  1.00  9.70           A    C
ANISOU 4101  CG  ARG A 669     1123   1216   1346    -41     82    -16  A    C
ATOM   4104  CD  ARG A 669       9.824 -13.310  10.535  1.00  9.29           A    C
ANISOU 4104  CD  ARG A 669     1160   1187   1180      8     41    -16  A    C
ATOM   4107  NE  ARG A 669      10.704 -13.141   9.382  1.00  9.73           A    N
ANISOU 4107  NE  ARG A 669     1108   1304   1282     47    121     17  A    N
ATOM   4109  CZ  ARG A 669      10.517 -12.283   8.391  1.00  8.76           A    C
ANISOU 4109  CZ  ARG A 669      976   1136   1215    -29     55     -8  A    C
ATOM   4110  NH1 ARG A 669       9.545 -11.374   8.457  1.00  9.89           A    N
ANISOU 4110  NH1 ARG A 669     1257   1069   1429    107     31     79  A    N
ATOM   4113  NH2 ARG A 669      11.321 -12.318   7.331  1.00  9.41           A    N
ANISOU 4113  NH2 ARG A 669      958   1356   1259     67    -25     14  A    N
ATOM   4116  C   ARG A 669       7.560 -17.057  12.966  1.00 11.24           A    C
ANISOU 4116  C   ARG A 669     1381   1382   1505    -24     40     46  A    C
ATOM   4117  O   ARG A 669       6.462 -17.362  12.504  1.00 12.43           A    O
ANISOU 4117  O   ARG A 669     1429   1678   1616     -7     -7     36  A    O
ATOM   4118  N   PRO A 670       7.777 -16.932  14.278  1.00 10.78           A    N
ANISOU 4118  N   PRO A 670     1358   1304   1433    -16     44     24  A    N
ATOM   4119  CA  PRO A 670       6.693 -17.121  15.258  1.00 11.05           A    C
ANISOU 4119  CA  PRO A 670     1382   1306   1508     94     74     11  A    C
ATOM   4121  CB  PRO A 670       7.395 -16.954  16.603  1.00 12.51           A    C
ANISOU 4121  CB  PRO A 670     1574   1557   1622     93    110    106  A    C
ATOM   4124  CG  PRO A 670       8.848 -17.065  16.308  1.00 14.02           A    C
ANISOU 4124  CG  PRO A 670     1667   1900   1757     32     29     37  A    C
ATOM   4127  CD  PRO A 670       9.038 -16.566  14.941  1.00 11.84           A    C
ANISOU 4127  CD  PRO A 670     1398   1492   1609     58     57    -14  A    C
ATOM   4130  C   PRO A 670       5.563 -16.085  15.124  1.00 10.64           A    C
ANISOU 4130  C   PRO A 670     1390   1262   1391     77     10     61  A    C
ATOM   4131  O   PRO A 670       5.789 -14.991  14.623  1.00 10.77           A    O
ANISOU 4131  O   PRO A 670     1372   1213   1505     26    100    103  A    O
ATOM   4132  N   ARG A 671       4.386 -16.459  15.610  1.00  9.98           A    N
ANISOU 4132  N   ARG A 671     1397   1118   1277     42     43     16  A    N
ATOM   4134  CA  ARG A 671       3.287 -15.549  15.845  1.00  9.83           A    C
ANISOU 4134  CA  ARG A 671     1239   1273   1221     17     15     41  A    C
ATOM   4136  CB  ARG A 671       2.003 -16.327  16.099  1.00 11.36           A    C
ANISOU 4136  CB  ARG A 671     1424   1436   1456    -26     58    -32  A    C
ATOM   4139  CG  ARG A 671       1.492 -17.209  14.990  1.00 11.68           A    C
ANISOU 4139  CG  ARG A 671     1487   1442   1507     -7     -2    -62  A    C
ATOM   4142  CD  ARG A 671       0.265 -17.961  15.456  1.00 13.47           A    C
ANISOU 4142  CD  ARG A 671     1545   1847   1724   -108    -54    -90  A    C
ATOM   4145  NE  ARG A 671      -0.454 -18.701  14.418  1.00 15.63           A    N
ANISOU 4145  NE  ARG A 671     2178   2005   1754    -61    -88   -169  A    N
ATOM   4147  CZ  ARG A 671      -0.352 -20.004  14.198  1.00 16.74           A    C
ANISOU 4147  CZ  ARG A 671     2188   2083   2090     38    -77    -75  A    C
ATOM   4148  NH1 ARG A 671       0.472 -20.772  14.900  1.00 16.43           A    N
ANISOU 4148  NH1 ARG A 671     2378   2055   1808    -56    -63    -72  A    N
ATOM   4151  NH2 ARG A 671      -1.099 -20.541  13.244  1.00 19.05           A    N
ANISOU 4151  NH2 ARG A 671     2530   2437   2270    -95   -158   -187  A    N
ATOM   4154  C   ARG A 671       3.548 -14.728  17.094  1.00  9.52           A    C
ANISOU 4154  C   ARG A 671     1255   1156   1204    -23     42     55  A    C
ATOM   4155  O   ARG A 671       4.253 -15.171  17.987  1.00  9.26           A    O
ANISOU 4155  O   ARG A 671     1265   1053   1199    -19     18     81  A    O
ATOM   4156  N   PHE A 672       2.968 -13.545  17.175  1.00  8.86           A    N
ANISOU 4156  N   PHE A 672     1187   1201    979     47     26    108  A    N
ATOM   4158  CA  PHE A 672       3.056 -12.781  18.411  1.00  9.06           A    C
ANISOU 4158  CA  PHE A 672     1203   1150   1088      1    -35      5  A    C
ATOM   4160  CB  PHE A 672       2.491 -11.371  18.298  1.00  8.73           A    C
ANISOU 4160  CB  PHE A 672     1134   1162   1019    -20    -23     15  A    C
ATOM   4163  CG  PHE A 672       3.413 -10.391  17.617  1.00  8.48           A    C
ANISOU 4163  CG  PHE A 672     1018   1176   1028     18     64    -38  A    C
ATOM   4164  CD1 PHE A 672       4.590  -9.994  18.243  1.00  7.89           A    C
ANISOU 4164  CD1 PHE A 672      930   1064   1001     43    -52    175  A    C
ATOM   4166  CE1 PHE A 672       5.453  -9.071  17.647  1.00  8.09           A    C
ANISOU 4166  CE1 PHE A 672      851   1131   1090     22     51     83  A    C
ATOM   4168  CZ  PHE A 672       5.128  -8.537  16.440  1.00  8.28           A    C
ANISOU 4168  CZ  PHE A 672      987   1081   1078     48    124     -9  A    C
ATOM   4170  CE2 PHE A 672       3.961  -8.912  15.811  1.00  7.94           A    C
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ANISOU 4170  CE2 PHE A 672     1007   1214    794     71     26     65  A    C
ATOM   4172  CD2 PHE A 672       3.093  -9.839  16.405  1.00  8.53       A    C
ANISOU 4172  CD2 PHE A 672      900   1101   1240    155     72     67  A    C
ATOM   4174  C   PHE A 672       2.434 -13.503  19.608  1.00  9.51       A    C
ANISOU 4174  C   PHE A 672     1260   1187   1165    -75    -10     25  A    C
ATOM   4175  O   PHE A 672       2.931 -13.344  20.712  1.00  9.70       A    O
ANISOU 4175  O   PHE A 672     1391   1234   1058     22     24     64  A    O
ATOM   4176  N   THR A 673       1.365 -14.279  19.415  1.00 10.26       A    N
ANISOU 4176  N   THR A 673     1338   1385   1174    -24    -79     13  A    N
ATOM   4178  CA  THR A 673       0.796 -15.017  20.538  1.00 11.04       A    C
ANISOU 4178  CA  THR A 673     1435   1416   1341    -90    -18    -35  A    C
ATOM   4180  CB  THR A 673      -0.429 -15.818  20.113  1.00 11.04       A    C
ANISOU 4180  CB  THR A 673     1462   1418   1314   -124     47    -10  A    C
ATOM   4182  OG1 THR A 673      -0.113 -16.572  18.929  1.00 12.62       A    O
ANISOU 4182  OG1 THR A 673     1749   1703   1342    -91     -1    -63  A    O
ATOM   4184  CG2 THR A 673      -1.572 -14.927  19.794  1.00 14.01       A    C
ANISOU 4184  CG2 THR A 673     1794   1912   1616    -96    -81    -17  A    C
ATOM   4188  C   THR A 673       1.832 -15.982  21.106  1.00 10.65       A    C
ANISOU 4188  C   THR A 673     1422   1377   1247    -87    -39    -32  A    C
ATOM   4189  O   THR A 673       1.945 -16.165  22.331  1.00 11.28       A    O
ANISOU 4189  O   THR A 673     1720   1470   1095    -84   -114    -35  A    O
ATOM   4190  N   GLU A 674       2.581 -16.610  20.215  1.00 10.28       A    N
ANISOU 4190  N   GLU A 674     1318   1415   1170    -66    -60    -48  A    N
ATOM   4192  CA  GLU A 674       3.604 -17.558  20.601  1.00  9.55       A    C
ANISOU 4192  CA  GLU A 674     1286   1171   1169    -95    -17     49  A    C
ATOM   4194  CB  GLU A 674       4.089 -18.337  19.379  1.00  9.92       A    C
ANISOU 4194  CB  GLU A 674     1261   1287   1218     11    -34     76  A    C
ATOM   4197  CG  GLU A 674       2.987 -19.163  18.766  1.00 10.67       A    C
ANISOU 4197  CG  GLU A 674     1529   1286   1240   -121    -59     77  A    C
ATOM   4200  CD  GLU A 674       3.274 -19.715  17.377  1.00 13.11       A    C
ANISOU 4200  CD  GLU A 674     1664   1734   1583   -101     61   -153  A    C
ATOM   4201  OE1 GLU A 674       4.217 -19.266  16.690  1.00 13.40       A    O
ANISOU 4201  OE1 GLU A 674     2084   1432   1573   -102    184    -21  A    O
ATOM   4202  OE2 GLU A 674       2.507 -20.632  16.978  1.00 13.86       A    O
ANISOU 4202  OE2 GLU A 674     2025   1710   1529   -255    -34    -61  A    O
ATOM   4203  C   GLU A 674       4.764 -16.849  21.313  1.00 10.35       A    C
ANISOU 4203  C   GLU A 674     1439   1212   1280    -51   -106     36  A    C
ATOM   4204  O   GLU A 674       5.255 -17.336  22.338  1.00 10.34       A    O
ANISOU 4204  O   GLU A 674     1523   1195   1208   -118   -224    -58  A    O
ATOM   4205  N   LEU A 675       5.140 -15.671  20.820  1.00  9.65       A    N
ANISOU 4205  N   LEU A 675     1316   1240   1110    -87    -64     54  A    N
ATOM   4207  CA  LEU A 675       6.188 -14.882  21.455  1.00  9.88       A    C
ANISOU 4207  CA  LEU A 675     1278   1213   1262    -26      0     16  A    C
ATOM   4209  CB  LEU A 675       6.548 -13.672  20.608  1.00  9.99       A    C
ANISOU 4209  CB  LEU A 675     1219   1193   1381    -28    -25    109  A    C
ATOM   4212  CG  LEU A 675       7.239 -13.975  19.315  1.00 11.68       A    C
ANISOU 4212  CG  LEU A 675     1357   1474   1605      1     -7    -59  A    C
ATOM   4214  CD1 LEU A 675       7.406 -12.708  18.480  1.00 11.63       A    C
ANISOU 4214  CD1 LEU A 675     1336   1609   1471     30     49    -12  A    C
ATOM   4218  CD2 LEU A 675       8.602 -14.677  19.558  1.00 13.00       A    C
ANISOU 4218  CD2 LEU A 675     1621   1429   1889    192    111     39  A    C
ATOM   4222  C   LEU A 675       5.784 -14.409  22.837  1.00  9.06       A    C
ANISOU 4222  C   LEU A 675     1220   1011   1211    -29    -10    -29  A    C
ATOM   4223  O   LEU A 675       6.635 -14.391  23.729  1.00  9.64       A    O
ANISOU 4223  O   LEU A 675     1264    999   1400   -121    -95    -31  A    O
ATOM   4224  N   VAL A 676       4.515 -14.065  23.036  1.00  8.74       A    N
ANISOU 4224  N   VAL A 676     1183   1015   1122    -11    -86     12  A    N
ATOM   4226  CA  VAL A 676       4.054 -13.684  24.378  1.00  9.18       A    C
ANISOU 4226  CA  VAL A 676     1202   1115   1170     14      0      7  A    C
ATOM   4228  CB  VAL A 676       2.565 -13.318  24.424  1.00  9.40       A    C
ANISOU 4228  CB  VAL A 676     1206   1125   1241    -70    -15      4  A    C
ATOM   4230  CG1 VAL A 676       2.078 -13.219  25.874  1.00  9.87       A    C
ANISOU 4230  CG1 VAL A 676     1297   1054   1396    -30     27    -38  A    C
ATOM   4234  CG2 VAL A 676       2.296 -12.008  23.707  1.00 10.69       A    C
ANISOU 4234  CG2 VAL A 676     1381   1261   1419     60     27     19  A    C
ATOM   4238  C   VAL A 676       4.329 -14.854  25.331  1.00  9.61       A    C
ANISOU 4238  C   VAL A 676     1309   1158   1182    -11    -20    -41  A    C
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ATOM   4239  O   VAL A 676       4.869 -14.665  26.407  1.00 10.06           A    O
ANISOU 4239  O   VAL A 676    1430   1231   1159     25    -91   -130  A    O
ATOM   4240  N   CYS A 677       3.982 -16.072  24.934  1.00  9.35           A    N
ANISOU 4240  N   CYS A 677    1252   1125   1172      1     17    -97  A    N
ATOM   4242  CA  CYS A 677       4.188 -17.218  25.804  1.00 10.25           A    C
ANISOU 4242  CA  CYS A 677    1352   1296   1245    -50    -30    -78  A    C
ATOM   4244  CB  CYS A 677       3.609 -18.447  25.185  1.00 10.64           A    C
ANISOU 4244  CB  CYS A 677    1398   1408   1236    -58    -63    -72  A    C
ATOM   4247  SG ACYS A 677       1.829 -18.464  25.115  0.50 13.52           A    S
ANISOU 4247  SG ACYS A 677    1551   1729   1857      0    -17   -204  A    S
ATOM   4248  SG BCYS A 677       3.228 -19.741  26.364  0.50 10.56           A    S
ANISOU 4248  SG BCYS A 677    1390   1399   1222   -109    107   -235  A    S
ATOM   4249  C   CYS A 677       5.666 -17.473  26.061  1.00  9.43           A    C
ANISOU 4249  C   CYS A 677    1285   1179   1117     12    -21    -31  A    C
ATOM   4250  O   CYS A 677       6.058 -17.707  27.201  1.00 10.05           A    O
ANISOU 4250  O   CYS A 677    1414   1194   1210   -153   -252    -36  A    O
ATOM   4251  N   SER A 678       6.486 -17.383  25.008  1.00  8.36           A    N
ANISOU 4251  N   SER A 678    1152   1066    955    -35    -75     27  A    N
ATOM   4253  CA  SER A 678       7.915 -17.600  25.138  1.00  9.06           A    C
ANISOU 4253  CA  SER A 678    1204   1113   1124    -61    -69    -12  A    C
ATOM   4255  CB  SER A 678       8.584 -17.543  23.793  1.00  9.26           A    C
ANISOU 4255  CB  SER A 678    1275   1086   1157    -61    -66    -68  A    C
ATOM   4258  OG  SER A 678       8.180 -18.653  23.002  1.00 12.08           A    O
ANISOU 4258  OG  SER A 678    1647   1513   1429   -130    -64   -419  A    O
ATOM   4260  C   SER A 678       8.534 -16.552  26.054  1.00  9.50           A    C
ANISOU 4260  C   SER A 678    1252   1205   1150    -13   -138    -17  A    C
ATOM   4261  O   SER A 678       9.335 -16.884  26.933  1.00  9.54           A    O
ANISOU 4261  O   SER A 678    1226   1317   1081     29   -338     33  A    O
ATOM   4262  N   LEU A 679       8.178 -15.298  25.863  1.00  9.02           A    N
ANISOU 4262  N   LEU A 679    1184   1158   1083    -49   -186     -6  A    N
ATOM   4264  CA  LEU A 679       8.752 -14.229  26.679  1.00  9.18           A    C
ANISOU 4264  CA  LEU A 679    1268   1121   1097    -22    -76    -27  A    C
ATOM   4266  CB  LEU A 679       8.417 -12.860  26.114  1.00  9.07           A    C
ANISOU 4266  CB  LEU A 679    1150   1116   1178    -20    -80    -62  A    C
ATOM   4269  CG  LEU A 679       9.285 -12.455  24.942  1.00 11.44           A    C
ANISOU 4269  CG  LEU A 679    1495   1415   1435    -16    -14     62  A    C
ATOM   4271  CD1 LEU A 679       8.711 -11.208  24.280  1.00 10.61           A    C
ANISOU 4271  CD1 LEU A 679    1316   1465   1250     45    -25    105  A    C
ATOM   4275  CD2 LEU A 679      10.694 -12.242  25.408  1.00 14.76           A    C
ANISOU 4275  CD2 LEU A 679    1710   1899   1997    -16    -45    124  A    C
ATOM   4279  C   LEU A 679       8.261 -14.341  28.110  1.00  9.19           A    C
ANISOU 4279  C   LEU A 679    1199   1164   1128    -49    -33    -33  A    C
ATOM   4280  O   LEU A 679       9.007 -14.024  29.021  1.00  9.17           A    O
ANISOU 4280  O   LEU A 679    1350   1097   1034    -88   -148    -73  A    O
ATOM   4281  N   SER A 680       7.040 -14.831  28.318  1.00  9.53           A    N
ANISOU 4281  N   SER A 680    1264   1260   1096   -104    -32    -73  A    N
ATOM   4283  CA  SER A 680       6.542 -15.069  29.662  1.00  9.87           A    C
ANISOU 4283  CA  SER A 680    1307   1230   1212    -48    -17      4  A    C
ATOM   4285  CB  SER A 680       5.084 -15.519  29.607  1.00 10.57           A    C
ANISOU 4285  CB  SER A 680    1323   1383   1309    -43     -9    -25  A    C
ATOM   4288  OG  SER A 680       4.254 -14.443  29.194  1.00 12.61           A    O
ANISOU 4288  OG  SER A 680    1503   1645   1642   -154      9    112  A    O
ATOM   4290  C   SER A 680       7.411 -16.120  30.370  1.00  9.74           A    C
ANISOU 4290  C   SER A 680    1253   1259   1187    -47    -65    -27  A    C
ATOM   4291  O   SER A 680       7.721 -15.995  31.552  1.00  9.65           A    O
ANISOU 4291  O   SER A 680    1260   1259   1145   -176   -159     11  A    O
ATOM   4292  N   ASP A 681       7.832 -17.128  29.622  1.00 10.22           A    N
ANISOU 4292  N   ASP A 681    1311   1310   1260    -95    -74    -21  A    N
ATOM   4294  CA  ASP A 681       8.692 -18.143  30.160  1.00 10.85           A    C
ANISOU 4294  CA  ASP A 681    1413   1376   1330    -58     15    -23  A    C
ATOM   4296  CB  ASP A 681       8.727 -19.322  29.206  1.00 11.85           A    C
ANISOU 4296  CB  ASP A 681    1502   1506   1493    -82    -23    -74  A    C
ATOM   4299  CG  ASP A 681       9.338 -20.518  29.799  1.00 16.25           A    C
ANISOU 4299  CG  ASP A 681    2172   1871   2130    -27    -50     15  A    C
ATOM   4300  OD1 ASP A 681       9.067 -20.848  30.985  1.00 19.17           A    O
ANISOU 4300  OD1 ASP A 681    2825   2056   2401    -98     37     95  A    O
ATOM   4301  OD2 ASP A 681      10.135 -21.197  29.137  1.00 22.71           A    O
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ANISOU 4301  OD2 ASP A 681     2860   2896   2873    100    287   -125  A    O
ATOM   4302  C   ASP A 681      10.093 -17.582  30.420  1.00  9.83        A    C
ANISOU 4302  C   ASP A 681     1291   1229   1214    -33     -9      3  A    C
ATOM   4303  O   ASP A 681      10.697 -17.870  31.453  1.00  9.52        A    O
ANISOU 4303  O   ASP A 681     1465   1109   1043   -208    -94    -14  A    O
ATOM   4304  N   VAL A 682      10.618 -16.755  29.524  1.00  9.45        A    N
ANISOU 4304  N   VAL A 682     1302   1248   1041    -17    -59    -27  A    N
ATOM   4306  CA  VAL A 682      11.932 -16.182  29.763  1.00  9.70        A    C
ANISOU 4306  CA  VAL A 682     1237   1272   1178     -1      0    -22  A    C
ATOM   4308  CB  VAL A 682      12.437 -15.382  28.542  1.00 10.01        A    C
ANISOU 4308  CB  VAL A 682     1269   1253   1281    -24     -8      3  A    C
ATOM   4310  CG1 VAL A 682      13.696 -14.604  28.873  1.00 11.04        A    C
ANISOU 4310  CG1 VAL A 682     1344   1480   1370    -33    -12   -103  A    C
ATOM   4314  CG2 VAL A 682      12.695 -16.309  27.344  1.00 11.13        A    C
ANISOU 4314  CG2 VAL A 682     1483   1482   1263     -9    -18    -15  A    C
ATOM   4318  C   VAL A 682      11.887 -15.289  31.013  1.00  8.96        A    C
ANISOU 4318  C   VAL A 682     1166   1175   1062     -9    -45     22  A    C
ATOM   4319  O   VAL A 682      12.817 -15.287  31.821  1.00  9.28        A    O
ANISOU 4319  O   VAL A 682     1190   1198   1138   -105    -21     12  A    O
ATOM   4320  N   TYR A 683      10.816 -14.515  31.149  1.00  7.42        A    N
ANISOU 4320  N   TYR A 683     1047    942    829    -59    -20    -35  A    N
ATOM   4322  CA  TYR A 683      10.624 -13.631  32.288  1.00  7.98        A    C
ANISOU 4322  CA  TYR A 683     1074   1004    953    -55      4    -19  A    C
ATOM   4324  CB  TYR A 683       9.360 -12.795  32.077  1.00  8.15        A    C
ANISOU 4324  CB  TYR A 683     1027    998   1070    -74     62    -36  A    C
ATOM   4327  CG  TYR A 683       9.083 -11.763  33.155  1.00  8.77        A    C
ANISOU 4327  CG  TYR A 683     1163   1096   1073    -18    -41    -62  A    C
ATOM   4328  CD1 TYR A 683      10.043 -10.838  33.534  1.00 10.84        A    C
ANISOU 4328  CD1 TYR A 683     1297   1445   1375    -80      0    -85  A    C
ATOM   4330  CE1 TYR A 683       9.781  -9.884  34.499  1.00 11.06        A    C
ANISOU 4330  CE1 TYR A 683     1495   1123   1581    -12      3    -24  A    C
ATOM   4332  CZ  TYR A 683       8.562  -9.838  35.089  1.00 12.24        A    C
ANISOU 4332  CZ  TYR A 683     1582   1372   1696    -55     14    -74  A    C
ATOM   4333  OH  TYR A 683       8.330  -8.897  36.057  1.00 15.28        A    O
ANISOU 4333  OH  TYR A 683     2259   1697   1848     56     92   -190  A    O
ATOM   4335  CE2 TYR A 683       7.570 -10.747  34.721  1.00 13.43        A    C
ANISOU 4335  CE2 TYR A 683     1604   1727   1768    -91    -83   -101  A    C
ATOM   4337  CD2 TYR A 683       7.847 -11.693  33.763  1.00 11.54        A    C
ANISOU 4337  CD2 TYR A 683     1252   1469   1663    -93     -2    -18  A    C
ATOM   4339  C   TYR A 683      10.565 -14.430  33.586  1.00  8.07        A    C
ANISOU 4339  C   TYR A 683     1051   1069    946   -108    -28    -44  A    C
ATOM   4340  O   TYR A 683      11.231 -14.062  34.562  1.00  7.95        A    O
ANISOU 4340  O   TYR A 683     1017   1108    894   -139   -233    -87  A    O
ATOM   4341  N   GLN A 684       9.791 -15.521  33.615  1.00  8.72        A    N
ANISOU 4341  N   GLN A 684     1095   1129   1086    -82    -76      7  A    N
ATOM   4343  CA  GLN A 684       9.722 -16.363  34.802  1.00  9.04        A    C
ANISOU 4343  CA  GLN A 684     1145   1183   1106    -53    -16     -3  A    C
ATOM   4345  CB  GLN A 684       8.733 -17.495  34.595  1.00  9.16        A    C
ANISOU 4345  CB  GLN A 684     1091   1195   1194    -26    -74     -3  A    C
ATOM   4348  CG  GLN A 684       8.473 -18.335  35.852  1.00 10.73        A    C
ANISOU 4348  CG  GLN A 684     1381   1285   1408   -113    -11     38  A    C
ATOM   4351  CD  GLN A 684       7.893 -17.496  36.997  1.00 12.42        A    C
ANISOU 4351  CD  GLN A 684     1633   1631   1454     28      7     39  A    C
ATOM   4352  OE1 GLN A 684       6.830 -16.884  36.841  1.00 16.82        A    O
ANISOU 4352  OE1 GLN A 684     1974   2086   2329    187     24   -137  A    O
ATOM   4353  NE2 GLN A 684       8.589 -17.457  38.133  1.00 14.35        A    N
ANISOU 4353  NE2 GLN A 684     1765   1983   1705   -164    -62     -2  A    N
ATOM   4356  C   GLN A 684      11.082 -16.929  35.138  1.00  8.57        A    C
ANISOU 4356  C   GLN A 684     1118   1150    987    -85    -69     23  A    C
ATOM   4357  O   GLN A 684      11.467 -16.964  36.312  1.00  8.94        A    O
ANISOU 4357  O   GLN A 684     1183   1310    901   -105   -146     57  A    O
ATOM   4358  N   MET A 685      11.819 -17.380  34.131  1.00 10.03        A    N
ANISOU 4358  N   MET A 685     1309   1375   1126    -90    -26     19  A    N
ATOM   4360  CA  MET A 685      13.137 -17.948  34.341  1.00 11.25        A    C
ANISOU 4360  CA  MET A 685     1465   1446   1360     23     -7     65  A    C
ATOM   4362  CB  MET A 685      13.759 -18.527  33.043  1.00 13.40        A    C
ANISOU 4362  CB  MET A 685     1718   1744   1630     41     31    -37  A    C
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ATOM   4365  CG  MET A 685      13.060 -19.717  32.372  1.00 19.86           A    C
ANISOU 4365  CG  MET A 685    2392   2405   2746   -124   -105    -80  A    C
ATOM   4368  SD  MET A 685      13.569 -19.901  30.581  1.00 29.53           A    S
ANISOU 4368  SD  MET A 685    3774   3826   3618   -102    214   -258  A    S
ATOM   4369  CE  MET A 685      15.286 -20.484  30.764  1.00 30.13           A    C
ANISOU 4369  CE  MET A 685    3856   3827   3763    -20     -5     -3  A    C
ATOM   4373  C   MET A 685      14.078 -16.898  34.926  1.00 11.10           A    C
ANISOU 4373  C   MET A 685    1418   1473   1327     37    -22     64  A    C
ATOM   4374  O   MET A 685      14.843 -17.202  35.835  1.00 11.04           A    O
ANISOU 4374  O   MET A 685    1410   1534   1248     44   -105    128  A    O
ATOM   4375  N   GLU A 686      14.019 -15.652  34.454  1.00 10.54           A    N
ANISOU 4375  N   GLU A 686    1324   1377   1302     67    -66     69  A    N
ATOM   4377  CA  GLU A 686      14.902 -14.607  34.994  1.00 11.48           A    C
ANISOU 4377  CA  GLU A 686    1494   1451   1415     17     -8     27  A    C
ATOM   4379  CB  GLU A 686      14.850 -13.339  34.134  1.00 12.27           A    C
ANISOU 4379  CB  GLU A 686    1590   1516   1552     56    -95     23  A    C
ATOM   4382  CG  GLU A 686      15.583 -13.464  32.816  1.00 15.45           A    C
ANISOU 4382  CG  GLU A 686    1974   2012   1882    -45     28     78  A    C
ATOM   4385  CD  GLU A 686      17.084 -13.665  32.979  1.00 17.34           A    C
ANISOU 4385  CD  GLU A 686    2104   2299   2185     23    -36    152  A    C
ATOM   4386  OE1 GLU A 686      17.705 -12.990  33.824  1.00 20.51           A    O
ANISOU 4386  OE1 GLU A 686    2696   2619   2476   -130     23     65  A    O
ATOM   4387  OE2 GLU A 686      17.639 -14.500  32.245  1.00 22.70           A    O
ANISOU 4387  OE2 GLU A 686    2785   3090   2748     69    102     19  A    O
ATOM   4388  C   GLU A 686      14.527 -14.269  36.433  1.00 11.50           A    C
ANISOU 4388  C   GLU A 686    1464   1491   1411     -1    -79    -46  A    C
ATOM   4389  O   GLU A 686      15.391 -13.952  37.250  1.00 12.04           A    O
ANISOU 4389  O   GLU A 686    1433   1693   1447    -23   -188    -23  A    O
ATOM   4390  N   LYS A 687      13.243 -14.314  36.756  1.00 11.63           A    N
ANISOU 4390  N   LYS A 687    1433   1604   1382    -14   -102    -46  A    N
ATOM   4392  CA  LYS A 687      12.819 -14.108  38.137  1.00 12.65           A    C
ANISOU 4392  CA  LYS A 687    1588   1684   1532    -16    -11    -87  A    C
ATOM   4394  CB  LYS A 687      11.299 -13.913  38.256  1.00 13.23           A    C
ANISOU 4394  CB  LYS A 687    1647   1753   1626    -37    -48    -64  A    C
ATOM   4397  CG  LYS A 687      10.854 -12.557  37.748  1.00 14.35           A    C
ANISOU 4397  CG  LYS A 687    1812   1849   1788    -32    -36    -65  A    C
ATOM   4400  CD  LYS A 687       9.432 -12.225  38.088  1.00 16.85           A    C
ANISOU 4400  CD  LYS A 687    2055   2179   2166     74     45    -58  A    C
ATOM   4403  CE  LYS A 687       8.451 -13.068  37.340  1.00 18.34           A    C
ANISOU 4403  CE  LYS A 687    2257   2306   2402      7     22   -106  A    C
ATOM   4406  NZ  LYS A 687       7.056 -12.575  37.590  1.00 19.25           A    N
ANISOU 4406  NZ  LYS A 687    2234   2532   2545     55    -32   -135  A    N
ATOM   4410  C   LYS A 687      13.299 -15.268  39.010  1.00 12.83           A    C
ANISOU 4410  C   LYS A 687    1596   1764   1513    -21    -27    -23  A    C
ATOM   4411  O   LYS A 687      13.721 -15.046  40.150  1.00 14.48           A    O
ANISOU 4411  O   LYS A 687    1839   2049   1612     -1    -81   -106  A    O
ATOM   4412  N   ASP A 688      13.308 -16.487  38.469  1.00 12.84           A    N
ANISOU 4412  N   ASP A 688    1627   1728   1522    -18      0     61  A    N
ATOM   4414  CA  ASP A 688      13.702 -17.672  39.237  1.00 14.56           A    C
ANISOU 4414  CA  ASP A 688    1861   1897   1773     10    -17     53  A    C
ATOM   4416  CB  ASP A 688      13.302 -18.968  38.521  1.00 14.83           A    C
ANISOU 4416  CB  ASP A 688    1929   1901   1803      4    -26     56  A    C
ATOM   4419  CG  ASP A 688      11.814 -19.206  38.505  1.00 16.42           A    C
ANISOU 4419  CG  ASP A 688    2103   2140   1993    -52      0     78  A    C
ATOM   4420  OD1 ASP A 688      11.063 -18.538  39.240  1.00 17.23           A    O
ANISOU 4420  OD1 ASP A 688    2223   2208   2113    -64     77    112  A    O
ATOM   4421  OD2 ASP A 688      11.307 -20.066  37.750  1.00 19.27           A    O
ANISOU 4421  OD2 ASP A 688    2544   2282   2494   -266     58    -12  A    O
ATOM   4422  C   ASP A 688      15.203 -17.739  39.502  1.00 15.66           A    C
ANISOU 4422  C   ASP A 688    1969   2053   1925     68    -73     52  A    C
ATOM   4423  O   ASP A 688      15.593 -18.395  40.463  1.00 15.79           A    O
ANISOU 4423  O   ASP A 688    1997   2210   1792     46   -105    206  A    O
ATOM   4424  N   ILE A 689      16.032 -17.093  38.677  1.00 18.10           A    N
ANISOU 4424  N   ILE A 689    2301   2353   2221     12    -20     53  A    N
ATOM   4426  CA  ILE A 689      17.498 -17.136  38.821  1.00 20.93           A    C
ANISOU 4426  CA  ILE A 689    2581   2724   2644     21    -41     11  A    C
ATOM   4428  CB  ILE A 689      18.220 -17.290  37.453  1.00 21.72           A    C
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ANISOU 4428  CB  ILE A 689     2673   2784   2795    -23     18    -28  A    C
ATOM   4430  CG1 ILE A 689      18.089 -16.038  36.614  1.00 21.57        A    C
ANISOU 4430  CG1 ILE A 689     2669   2823   2700     17    -34    -36  A    C
ATOM   4433  CD1 ILE A 689      19.026 -15.997  35.454  1.00 22.85        A    C
ANISOU 4433  CD1 ILE A 689     2820   2972   2889     -4     60    -13  A    C
ATOM   4437  CG2 ILE A 689      17.710 -18.490  36.694  1.00 22.88        A    C
ANISOU 4437  CG2 ILE A 689     2908   2946   2839    -11      8    -91  A    C
ATOM   4441  C   ILE A 689      18.087 -15.913  39.530  1.00 23.30        A    C
ANISOU 4441  C   ILE A 689     2912   2957   2984    -36    -22    -17  A    C
ATOM   4442  O   ILE A 689      19.277 -15.920  39.902  1.00 23.81        A    O
ANISOU 4442  O   ILE A 689     2927   3059   3058    -22    -29     37  A    O
ATOM   4443  N   ALA A 690      17.262 -14.881  39.710  1.00 25.55        A    N
ANISOU 4443  N   ALA A 690     3207   3235   3264     20     -2     20  A    N
ATOM   4445  CA  ALA A 690      17.618 -13.679  40.471  1.00 27.12        A    C
ANISOU 4445  CA  ALA A 690     3435   3420   3448    -18     -3    -27  A    C
ATOM   4447  CB  ALA A 690      16.581 -12.595  40.243  1.00 27.19        A    C
ANISOU 4447  CB  ALA A 690     3445   3474   3410      1      3      6  A    C
ATOM   4451  C   ALA A 690      17.747 -13.963  41.968  1.00 28.89        A    C
ANISOU 4451  C   ALA A 690     3685   3655   3634     -5      5    -10  A    C
ATOM   4452  O   ALA A 690      16.742 -14.025  42.694  1.00 28.87        A    O
ANISOU 4452  O   ALA A 690     3666   3645   3656    -33    -33    -25  A    O
ATOM   4453  N   MET A 691      18.996 -14.135  42.405  1.00 30.85        A    N
ANISOU 4453  N   MET A 691     3873   3933   3914     -5    -14    -11  A    N
ATOM   4455  CA  MET A 691      19.370 -14.457  43.786  1.00 32.32        A    C
ANISOU 4455  CA  MET A 691     4087   4098   4091      1    -19     27  A    C
ATOM   4457  CB  MET A 691      18.774 -13.495  44.826  1.00 33.00        A    C
ANISOU 4457  CB  MET A 691     4151   4222   4164    -11      3    -11  A    C
ATOM   4460  CG  MET A 691      18.728 -12.016  44.416  1.00 35.89        A    C
ANISOU 4460  CG  MET A 691     4550   4476   4609    -31    -30     84  A    C
ATOM   4463  SD  MET A 691      18.072 -10.919  45.716  1.00 40.73        A    S
ANISOU 4463  SD  MET A 691     5194   5075   5207     38     82    -71  A    S
ATOM   4464  CE  MET A 691      17.146  -9.766  44.717  1.00 40.93        A    C
ANISOU 4464  CE  MET A 691     5182   5149   5218     11     18     19  A    C
ATOM   4468  C   MET A 691      18.924 -15.883  44.029  1.00 32.38        A    C
ANISOU 4468  C   MET A 691     4093   4096   4113     -9     -3     42  A    C
ATOM   4469  O   MET A 691      19.736 -16.802  44.132  1.00 33.00        A    O
ANISOU 4469  O   MET A 691     4199   4106   4234     -3     58     28  A    O
ATOM   4470  OXT MET A 691      17.733 -16.130  44.091  1.00 32.92        A    O
ANISOU 4470  OXT MET A 691     4172   4147   4189      3    -42     56  A    O
ATOM   4471 AS   AS  C 459      -3.095  18.704  14.731  0.50 33.56        C   AS
ATOM   4472 AS   AS  C 677       1.446 -19.607  27.573  0.50 35.18        C   AS
ATOM   4473  O   HOH W   1      19.479  -9.528  13.063  1.00 13.87        W    O
ATOM   4476  O   HOH W   2      16.961  -5.517  10.992  1.00 15.15        W    O
ATOM   4479  O   HOH W   3       6.300  -4.344   9.624  1.00 15.98        W    O
ATOM   4482  O   HOH W   4      24.481  -5.000  22.089  1.00 17.95        W    O
ATOM   4485  O   HOH W   5      14.777   3.240  18.099  1.00 15.35        W    O
ATOM   4488  O   HOH W   6      23.760  -5.968  26.879  1.00 16.90        W    O
ATOM   4491  O   HOH W   7       1.042  -6.829  13.337  1.00 18.66        W    O
ATOM   4494  O   HOH W   8      19.751  -2.578   2.644  1.00 20.13        W    O
ATOM   4497  O   HOH W   9      17.092  -4.813   8.543  1.00 15.12        W    O
ATOM   4500  O   HOH W  10      -4.221   2.343  24.689  1.00 19.64        W    O
ATOM   4503  O   HOH W  11      18.305   2.556  18.877  1.00 18.58        W    O
ATOM   4506  O   HOH W  12      -7.953  -9.648  20.392  1.00 17.80        W    O
ATOM   4509  O   HOH W  13      17.994   2.499   9.123  1.00 18.39        W    O
ATOM   4512  O   HOH W  14      14.790   6.896  22.565  1.00 16.75        W    O
ATOM   4515  O   HOH W  15      27.168  -8.111  21.389  1.00 17.65        W    O
ATOM   4518  O   HOH W  16      -0.333  -9.332   7.954  1.00 21.84        W    O
ATOM   4521  O   HOH W  17      -2.677  18.484  -2.169  1.00 21.93        W    O
ATOM   4524  O   HOH W  18      15.551  -2.808  37.019  1.00 18.87        W    O
ATOM   4527  O   HOH W  19       4.454  -2.679  -1.326  1.00 19.19        W    O
ATOM   4530  O   HOH W  20      10.008  -5.335   9.247  1.00 23.00        W    O
ATOM   4533  O   HOH W  21      25.415  -5.343  24.575  1.00 21.32        W    O
ATOM   4536  O   HOH W  22      13.461   9.250  27.873  1.00 18.51        W    O
ATOM   4539  O   HOH W  23      26.898 -11.622  23.911  1.00 23.24        W    O
ATOM   4542  O   HOH W  24      18.133 -15.564  12.221  1.00 21.74        W    O
ATOM   4545  O   HOH W  25      12.105 -12.266   3.348  1.00 17.80        W    O
ATOM   4548  O   HOH W  26      -0.257 -15.874  24.048  1.00 23.98        W    O
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ATOM	4551	O	HOH	W	27	13.196	0.899	35.037	1.00	21.23	W	O
ATOM	4554	O	HOH	W	28	0.840	-21.860	18.764	1.00	21.06	W	O
ATOM	4557	O	HOH	W	29	17.583	-9.596	36.668	1.00	19.88	W	O
ATOM	4560	O	HOH	W	30	-2.774	-12.358	18.133	1.00	19.66	W	O
ATOM	4563	O	HOH	W	31	4.584	-14.069	12.249	1.00	21.22	W	O
ATOM	4566	O	HOH	W	32	23.562	-4.487	0.477	1.00	22.27	W	O
ATOM	4569	O	HOH	W	33	26.010	-13.571	18.980	1.00	22.84	W	O
ATOM	4572	O	HOH	W	34	9.525	-6.939	37.377	1.00	27.84	W	O
ATOM	4575	O	HOH	W	35	-2.681	2.630	27.804	1.00	21.91	W	O
ATOM	4578	O	HOH	W	36	4.342	12.092	26.768	1.00	24.91	W	O
ATOM	4581	O	HOH	W	37	7.984	-18.825	20.209	1.00	25.15	W	O
ATOM	4584	O	HOH	W	38	18.468	4.977	22.255	1.00	22.38	W	O
ATOM	4587	O	HOH	W	39	14.159	-19.657	23.215	1.00	21.41	W	O
ATOM	4590	O	HOH	W	40	0.586	-0.637	8.269	1.00	24.36	W	O
ATOM	4593	O	HOH	W	41	2.295	11.344	25.221	1.00	27.87	W	O
ATOM	4596	O	HOH	W	42	-7.451	21.442	33.821	1.00	27.32	W	O
ATOM	4599	O	HOH	W	43	-3.039	25.687	20.469	1.00	24.75	W	O
ATOM	4602	O	HOH	W	44	3.160	-23.086	16.130	1.00	27.74	W	O
ATOM	4605	O	HOH	W	45	17.028	-17.456	7.945	1.00	23.83	W	O
ATOM	4608	O	HOH	W	46	-4.639	26.435	28.046	1.00	31.05	W	O
ATOM	4611	O	HOH	W	47	-10.923	-5.627	20.143	1.00	22.57	W	O
ATOM	4614	O	HOH	W	48	19.351	-18.606	28.704	1.00	28.51	W	O
ATOM	4617	O	HOH	W	49	21.847	-11.720	31.609	1.00	26.04	W	O
ATOM	4620	O	HOH	W	50	10.662	-4.033	-5.247	1.00	31.05	W	O
ATOM	4623	O	HOH	W	51	20.457	-8.195	36.064	1.00	27.03	W	O
ATOM	4626	O	HOH	W	52	-3.376	22.364	15.888	1.00	25.70	W	O
ATOM	4629	O	HOH	W	53	-2.265	-15.175	15.979	1.00	29.94	W	O
ATOM	4632	O	HOH	W	54	-2.279	-8.980	24.279	1.00	26.59	W	O
ATOM	4635	O	HOH	W	55	11.181	3.524	-1.057	1.00	22.83	W	O
ATOM	4638	O	HOH	W	56	17.643	-12.520	36.367	1.00	27.57	W	O
ATOM	4641	O	HOH	W	57	1.623	1.370	10.079	1.00	25.21	W	O
ATOM	4644	O	HOH	W	58	15.664	-13.804	45.226	1.00	34.15	W	O
ATOM	4647	O	HOH	W	59	6.256	-9.797	37.610	1.00	34.43	W	O
ATOM	4650	O	HOH	W	60	25.815	-12.306	14.831	1.00	27.33	W	O
ATOM	4653	O	HOH	W	61	5.824	-14.786	33.356	1.00	25.11	W	O
ATOM	4656	O	HOH	W	62	16.873	-4.248	-1.845	1.00	32.13	W	O
ATOM	4659	O	HOH	W	63	5.848	-20.107	12.441	1.00	26.50	W	O
ATOM	4662	O	HOH	W	64	14.032	24.397	19.568	1.00	36.45	W	O
ATOM	4665	O	HOH	W	65	12.803	-10.837	0.729	1.00	28.65	W	O
ATOM	4668	O	HOH	W	66	13.165	9.672	0.079	1.00	33.59	W	O
ATOM	4671	O	HOH	W	67	16.453	-17.500	33.129	1.00	24.48	W	O
ATOM	4674	O	HOH	W	68	2.439	17.984	17.888	1.00	22.03	W	O
ATOM	4677	O	HOH	W	69	11.257	-4.973	36.931	1.00	28.56	W	O
ATOM	4680	O	HOH	W	70	11.119	4.907	15.842	1.00	35.29	W	O
ATOM	4683	O	HOH	W	71	6.008	-10.532	5.341	1.00	24.54	W	O
ATOM	4686	O	HOH	W	72	-2.020	23.984	11.556	1.00	28.27	W	O
ATOM	4689	O	HOH	W	73	5.919	-14.701	35.857	1.00	34.04	W	O
ATOM	4692	O	HOH	W	74	8.884	-0.202	8.933	1.00	24.05	W	O
ATOM	4695	O	HOH	W	75	-9.784	22.893	33.258	1.00	34.77	W	O
ATOM	4698	O	HOH	W	76	6.001	5.485	2.908	1.00	34.66	W	O
ATOM	4701	O	HOH	W	77	5.311	-21.415	10.117	1.00	27.03	W	O
ATOM	4704	O	HOH	W	78	23.051	3.901	2.619	1.00	27.45	W	O
ATOM	4707	O	HOH	W	79	8.600	25.383	26.603	1.00	34.39	W	O
ATOM	4710	O	HOH	W	80	3.627	-20.342	13.945	1.00	28.33	W	O
ATOM	4713	O	HOH	W	81	-6.693	-5.138	9.294	1.00	27.84	W	O
ATOM	4716	O	HOH	W	82	26.573	-7.308	10.342	1.00	30.01	W	O
ATOM	4719	O	HOH	W	83	18.225	-7.928	-2.386	1.00	29.57	W	O
ATOM	4722	O	HOH	W	84	-2.632	-9.217	9.188	1.00	35.57	W	O
ATOM	4725	O	HOH	W	85	24.388	5.011	8.985	1.00	38.75	W	O
ATOM	4728	O	HOH	W	86	-2.044	-18.488	18.517	1.00	25.55	W	O
ATOM	4731	O	HOH	W	87	20.358	-12.721	33.680	1.00	34.51	W	O
ATOM	4734	O	HOH	W	88	21.485	-18.154	22.079	1.00	32.93	W	O
ATOM	4737	O	HOH	W	89	-8.489	-10.513	12.287	1.00	52.27	W	O
ATOM	4740	O	HOH	W	90	-14.058	25.192	26.302	1.00	37.49	W	O
ATOM	4743	O	HOH	W	91	-8.604	-12.364	15.709	1.00	27.58	W	O
ATOM	4746	O	HOH	W	92	1.743	-13.653	12.892	1.00	27.13	W	O
ATOM	4749	O	HOH	W	93	-14.328	5.985	16.063	1.00	35.97	W	O

ATOM	4752	O	HOH W	94	5.089	-4.158	35.982	1.00	32.25	W	O
ATOM	4755	O	HOH W	95	2.555	-18.427	6.350	1.00	46.30	W	O
ATOM	4758	O	HOH W	96	-6.583	24.083	13.571	1.00	32.28	W	O
ATOM	4761	O	HOH W	97	3.120	-6.286	32.922	1.00	28.76	W	O
ATOM	4764	O	HOH W	98	12.911	-20.364	20.813	1.00	32.18	W	O
ATOM	4767	O	HOH W	99	9.662	-20.723	23.943	1.00	28.10	W	O
ATOM	4770	O	HOH W	100	29.818	2.171	8.058	1.00	38.15	W	O
ATOM	4773	O	HOH W	101	22.923	4.746	34.609	1.00	28.23	W	O
ATOM	4776	O	HOH W	102	18.586	5.476	3.189	1.00	32.67	W	O
ATOM	4779	O	HOH W	103	23.350	2.836	26.154	1.00	29.63	W	O
ATOM	4782	O	HOH W	104	-14.292	5.543	20.132	1.00	40.05	W	O
ATOM	4785	O	HOH W	105	21.006	-1.829	-1.022	1.00	33.79	W	O
ATOM	4788	O	HOH W	106	25.675	-13.300	12.460	1.00	31.34	W	O
ATOM	4791	O	HOH W	107	-14.390	18.999	19.688	1.00	40.08	W	O
ATOM	4794	O	HOH W	108	15.107	-0.283	0.138	1.00	24.96	W	O
ATOM	4797	O	HOH W	109	21.210	4.757	9.005	1.00	47.23	W	O
ATOM	4800	O	HOH W	110	18.421	10.903	28.240	1.00	37.02	W	O
ATOM	4803	O	HOH W	111	-6.564	5.275	23.280	1.00	40.82	W	O
ATOM	4806	O	HOH W	112	-11.988	7.492	39.713	1.00	32.17	W	O
ATOM	4809	O	HOH W	113	0.944	-3.471	5.721	1.00	32.52	W	O
ATOM	4812	O	HOH W	114	6.227	2.802	3.217	1.00	26.41	W	O
ATOM	4815	O	HOH W	115	3.619	0.859	39.059	1.00	56.40	W	O
ATOM	4818	O	HOH W	116	26.615	-5.575	2.785	1.00	34.50	W	O
ATOM	4821	O	HOH W	117	5.391	6.091	14.350	1.00	28.96	W	O
ATOM	4824	O	HOH W	118	8.361	18.917	31.821	1.00	54.83	W	O
ATOM	4827	O	HOH W	119	27.592	-5.870	29.687	1.00	34.00	W	O
ATOM	4830	O	HOH W	120	26.393	-9.066	12.033	1.00	34.61	W	O
ATOM	4833	O	HOH W	121	24.039	4.111	28.493	1.00	49.57	W	O
ATOM	4836	O	HOH W	122	0.385	10.038	33.013	1.00	43.66	W	O
ATOM	4839	O	HOH W	123	-1.581	28.019	31.964	1.00	42.03	W	O
ATOM	4842	O	HOH W	124	-0.402	18.593	1.186	1.00	33.08	W	O
ATOM	4845	O	HOH W	125	-14.153	22.528	22.865	1.00	39.67	W	O
ATOM	4848	O	HOH W	126	1.422	19.788	5.361	1.00	33.75	W	O
ATOM	4851	O	HOH W	127	6.159	2.368	5.998	1.00	30.29	W	O
ATOM	4854	O	HOH W	128	21.291	-16.934	9.903	1.00	45.24	W	O
ATOM	4857	O	HOH W	129	0.770	-6.150	31.663	1.00	42.18	W	O
ATOM	4860	O	HOH W	130	-4.043	-12.320	12.617	1.00	42.29	W	O
ATOM	4863	O	HOH W	131	20.383	9.724	26.884	1.00	36.62	W	O
ATOM	4866	O	HOH W	132	-2.168	11.721	35.512	1.00	40.29	W	O
ATOM	4869	O	HOH W	133	15.005	2.551	-1.347	1.00	32.89	W	O
ATOM	4872	O	HOH W	134	8.794	-21.009	38.199	1.00	46.17	W	O
ATOM	4875	O	HOH W	135	2.518	-13.122	30.733	1.00	38.37	W	O
ATOM	4878	O	HOH W	136	7.635	-12.706	1.407	1.00	29.71	W	O
ATOM	4881	O	HOH W	137	-8.685	24.816	12.760	1.00	44.11	W	O
ATOM	4884	O	HOH W	138	-2.636	-3.254	8.677	1.00	27.21	W	O
ATOM	4887	O	HOH W	139	15.768	-18.358	12.147	1.00	40.67	W	O
ATOM	4890	O	HOH W	140	10.814	24.683	22.492	1.00	32.90	W	O
ATOM	4893	O	HOH W	141	28.656	-9.702	31.405	1.00	50.52	W	O
ATOM	4896	O	HOH W	142	-6.161	-0.734	28.566	1.00	35.85	W	O
ATOM	4899	O	HOH W	143	26.107	4.685	13.078	1.00	36.41	W	O
ATOM	4902	O	HOH W	144	-14.326	16.032	30.233	1.00	40.43	W	O
ATOM	4905	O	HOH W	145	25.066	-1.521	25.107	1.00	34.70	W	O
ATOM	4908	O	HOH W	146	13.051	11.026	25.453	1.00	34.11	W	O
ATOM	4911	O	HOH W	147	1.206	9.609	20.300	1.00	50.37	W	O
ATOM	4914	O	HOH W	148	-8.334	7.205	5.910	1.00	50.55	W	O
ATOM	4917	O	HOH W	149	2.947	1.838	36.508	1.00	46.93	W	O
ATOM	4920	O	HOH W	150	21.572	-18.163	40.127	1.00	45.84	W	O
ATOM	4923	O	HOH W	151	7.365	17.383	10.315	1.00	54.72	W	O
ATOM	4926	O	HOH W	152	0.176	-7.017	4.002	1.00	44.22	W	O
ATOM	4929	O	HOH W	153	19.073	6.380	37.289	1.00	31.56	W	O
ATOM	4932	O	HOH W	154	5.202	16.145	34.778	1.00	54.68	W	O
ATOM	4935	O	HOH W	155	23.720	5.441	13.483	1.00	32.64	W	O
ATOM	4938	O	HOH W	156	16.401	5.555	7.238	1.00	36.23	W	O
ATOM	4941	O	HOH W	157	-6.498	14.764	40.845	1.00	40.96	W	O
ATOM	4944	O	HOH W	158	28.600	0.254	-2.197	1.00	53.63	W	O
ATOM	4947	O	HOH W	159	-12.018	32.218	16.285	1.00	49.07	W	O
ATOM	4950	O	HOH W	160	0.086	5.373	33.101	1.00	51.51	W	O

ATOM	4953	O	HOH W 161	3.274	8.583	10.649	1.00	43.06	W	O
ATOM	4956	O	HOH W 162	22.605	-15.423	14.524	1.00	41.77	W	O
ATOM	4959	O	HOH W 163	-8.630	18.199	6.540	1.00	27.18	W	O
ATOM	4962	O	HOH W 164	-8.686	-8.527	8.537	1.00	37.06	W	O
ATOM	4965	O	HOH W 165	17.356	5.561	-7.220	1.00	41.21	W	O
ATOM	4968	O	HOH W 166	3.075	32.008	7.880	1.00	40.35	W	O
ATOM	4971	O	HOH W 167	1.196	5.617	4.183	1.00	45.38	W	O
ATOM	4974	O	HOH W 168	17.656	-7.868	12.209	1.00	15.06	W	O
ATOM	4977	O	HOH W 169	8.664	-2.770	9.648	1.00	17.79	W	O
ATOM	4980	O	HOH W 170	16.832	4.787	18.630	1.00	23.56	W	O
ATOM	4983	O	HOH W 171	25.819	-2.202	22.551	1.00	29.20	W	O
ATOM	4986	O	HOH W 172	16.837	6.486	20.798	1.00	27.27	W	O
ATOM	4989	O	HOH W 173	27.727	-6.757	23.692	1.00	26.70	W	O
ATOM	4992	O	HOH W 174	2.136	34.684	8.355	1.00	27.14	W	O
ATOM	4995	O	HOH W 175	14.492	-0.335	37.262	1.00	31.03	W	O
ATOM	4998	O	HOH W 176	-3.745	-17.152	16.943	1.00	33.32	W	O
ATOM	5001	O	HOH W 177	-1.756	-18.155	23.813	1.00	32.25	W	O
ATOM	5004	O	HOH W 178	25.489	-4.554	28.614	1.00	23.71	W	O
ATOM	5007	O	HOH W 179	-2.274	20.476	-0.391	1.00	28.26	W	O
ATOM	5010	O	HOH W 180	15.514	-22.083	23.613	1.00	31.71	W	O
ATOM	5013	O	HOH W 181	-1.046	-11.416	25.140	1.00	31.45	W	O
ATOM	5016	O	HOH W 182	-2.632	28.253	21.086	1.00	32.74	W	O
ATOM	5019	O	HOH W 183	11.904	-19.349	24.906	1.00	30.37	W	O
ATOM	5022	O	HOH W 184	32.998	2.770	8.818	1.00	46.53	W	O
ATOM	5025	O	HOH W 185	28.730	-4.730	4.511	1.00	41.03	W	O
ATOM	5028	O	HOH W 186	-1.306	-13.421	23.428	1.00	30.60	W	O
ATOM	5031	O	HOH W 187	-5.846	-9.685	22.266	1.00	42.87	W	O
ATOM	5034	O	HOH W 188	18.729	-2.113	0.135	1.00	31.07	W	O
ATOM	5037	O	HOH W 189	13.762	4.268	15.601	1.00	27.23	W	O
ATOM	5040	O	HOH W 190	29.119	-10.372	25.129	1.00	31.33	W	O
ATOM	5043	O	HOH W 191	18.260	-17.081	10.290	1.00	35.26	W	O
ATOM	5046	O	HOH W 192	-1.716	-21.180	18.016	1.00	32.32	W	O
ATOM	5049	O	HOH W 193	20.664	-16.507	13.211	1.00	32.95	W	O
ATOM	5052	O	HOH W 194	7.956	2.015	7.876	1.00	33.80	W	O
ATOM	5055	O	HOH W 195	4.019	15.799	17.163	1.00	33.98	W	O
ATOM	5058	O	HOH W 196	10.942	-21.613	4.110	1.00	40.01	W	O
ATOM	5061	O	HOH W 197	15.808	24.518	17.442	1.00	34.61	W	O
ATOM	5064	O	HOH W 198	-15.812	12.856	34.586	1.00	57.34	W	O
ATOM	5067	O	HOH W 199	4.936	-12.559	3.726	1.00	31.32	W	O
ATOM	5070	O	HOH W 200	15.915	-16.350	31.154	1.00	40.13	W	O
ATOM	5073	O	HOH W 201	10.572	-13.606	1.569	1.00	32.28	W	O
ATOM	5076	O	HOH W 202	20.085	7.998	21.383	1.00	47.13	W	O
ATOM	5079	O	HOH W 203	-1.727	-3.536	6.311	1.00	40.15	W	O
ATOM	5082	O	HOH W 204	28.069	-13.639	22.482	1.00	38.00	W	O
ATOM	5085	O	HOH W 205	2.428	8.130	33.485	1.00	56.76	W	O
ATOM	5088	O	HOH W 206	4.112	7.796	19.654	1.00	43.60	W	O
ATOM	5091	O	HOH W 207	-16.832	18.512	28.867	1.00	43.33	W	O
ATOM	5094	O	HOH W 208	4.438	6.672	36.992	1.00	49.89	W	O
ATOM	5097	O	HOH W 209	24.369	-10.892	0.049	1.00	36.67	W	O
ATOM	5100	O	HOH W 210	20.567	-12.279	41.840	1.00	45.28	W	O
ATOM	5103	O	HOH W 211	23.638	-17.238	22.606	1.00	38.24	W	O
ATOM	5106	O	HOH W 212	22.584	4.986	6.358	1.00	40.70	W	O
ATOM	5109	O	HOH W 213	-12.649	13.319	22.068	1.00	32.40	W	O
ATOM	5112	O	HOH W 214	7.869	-4.780	37.501	1.00	43.91	W	O
ATOM	5115	O	HOH W 215	22.264	-16.129	40.997	1.00	39.04	W	O
ATOM	5118	O	HOH W 216	7.155	-17.336	2.301	1.00	39.75	W	O
ATOM	5121	O	HOH W 217	-9.374	10.623	2.581	1.00	46.78	W	O
ATOM	5124	O	HOH W 218	-9.826	6.624	11.499	1.00	34.26	W	O
ATOM	5127	O	HOH W 219	-8.295	-12.287	20.270	1.00	39.42	W	O
ATOM	5130	O	HOH W 220	22.830	-14.126	30.372	1.00	46.91	W	O
ATOM	5133	O	HOH W 221	-3.842	27.866	25.606	1.00	34.41	W	O
ATOM	5136	O	HOH W 222	-14.473	7.008	39.365	1.00	36.88	W	O
ATOM	5139	O	HOH W 223	-13.757	24.696	33.168	1.00	42.28	W	O
ATOM	5142	O	HOH W 224	-5.644	16.691	42.105	1.00	41.39	W	O
ATOM	5145	O	HOH W 225	25.497	5.411	36.898	1.00	48.15	W	O
ATOM	5148	O	HOH W 226	27.283	5.516	9.317	1.00	46.59	W	O
ATOM	5151	O	HOH W 227	29.498	4.434	1.020	1.00	58.47	W	O

ATOM	5154	O	HOH W 228	3.321	-8.425	31.429	1.00	43.70	W	O
ATOM	5157	O	HOH W 229	24.117	-15.190	12.199	1.00	41.18	W	O
ATOM	5160	O	HOH W 230	20.124	-12.389	37.708	1.00	36.53	W	O
ATOM	5163	O	HOH W 231	-9.229	-1.501	21.266	1.00	28.25	W	O
ATOM	5166	O	HOH W 232	-15.779	25.297	28.169	1.00	44.87	W	O
ATOM	5169	O	HOH W 233	-0.796	-15.490	26.671	1.00	35.65	W	O
ATOM	5172	O	HOH W 234	-7.531	25.852	28.118	1.00	39.03	W	O
ATOM	5175	O	HOH W 235	21.351	4.652	37.194	1.00	34.74	W	O
ATOM	5178	O	HOH W 236	-10.908	11.891	7.021	1.00	50.12	W	O
ATOM	5181	O	HOH W 237	20.093	-19.985	39.619	1.00	41.48	W	O
ATOM	5184	O	HOH W 238	16.913	1.636	0.158	1.00	57.66	W	O
ATOM	5187	O	HOH W 239	24.550	-11.786	32.361	1.00	45.44	W	O
ATOM	5190	O	HOH W 240	6.951	12.068	26.595	1.00	46.84	W	O
ATOM	5193	O	HOH W 241	-2.373	24.816	15.700	1.00	32.54	W	O
ATOM	5196	O	HOH W 242	-0.321	-13.885	29.001	1.00	46.53	W	O
ATOM	5199	O	HOH W 243	11.563	-21.031	35.283	1.00	45.62	W	O
ATOM	5202	O	HOH W 244	18.288	-21.396	23.711	1.00	35.24	W	O
ATOM	5205	O	HOH W 245	22.670	-5.732	-1.765	1.00	40.51	W	O
ATOM	5208	O	HOH W 246	12.161	-20.481	27.378	1.00	40.97	W	O
ATOM	5211	O	HOH W 247	16.743	-19.964	16.894	1.00	46.39	W	O
ATOM	5214	O	HOH W 248	19.872	-15.776	32.453	1.00	41.59	W	O
ATOM	5217	O	HOH W 249	-14.124	23.466	20.534	1.00	45.11	W	O
ATOM	5220	O	HOH W 250	29.513	0.952	5.819	1.00	51.70	W	O
ATOM	5223	O	HOH W 251	18.691	-2.032	40.376	1.00	45.89	W	O
ATOM	5226	O	HOH W 252	10.687	1.887	-7.837	1.00	42.18	W	O
ATOM	5229	O	HOH W 253	12.119	-2.579	-7.064	1.00	40.90	W	O
ATOM	5232	O	HOH W 254	5.119	26.162	2.725	1.00	46.48	W	O
ATOM	5235	O	HOH W 255	1.481	20.173	33.847	1.00	38.28	W	O
ATOM	5238	O	HOH W 256	10.507	8.862	0.082	1.00	42.31	W	O
ATOM	5241	O	HOH W 257	25.796	6.387	-1.577	1.00	53.89	W	O
ATOM	5244	O	HOH W 258	20.185	1.064	-1.864	1.00	46.15	W	O
ATOM	5247	O	HOH W 259	-12.742	25.526	20.010	1.00	51.93	W	O
ATOM	5250	O	HOH W 260	21.887	8.253	14.036	1.00	62.78	W	O
ATOM	5253	O	HOH W 261	-10.680	10.655	33.008	1.00	44.00	W	O
ATOM	5256	O	HOH W 262	-6.574	8.507	31.016	1.00	46.18	W	O
ATOM	5259	O	HOH W 263	3.942	-12.795	33.099	1.00	40.21	W	O
ATOM	5262	O	HOH W 264	1.018	17.787	33.485	1.00	38.43	W	O
ATOM	5265	O	HOH W 265	26.837	3.753	28.570	1.00	46.62	W	O
ATOM	5268	O	HOH W 266	7.159	-23.096	9.113	1.00	37.42	W	O
ATOM	5271	O	HOH W 267	12.960	13.454	3.068	1.00	71.06	W	O
ATOM	5274	O	HOH W 268	22.282	9.259	28.712	1.00	43.17	W	O
ATOM	5277	O	HOH W 269	9.738	17.174	27.040	1.00	53.53	W	O
ATOM	5280	O	HOH W 270	26.067	-5.231	0.124	1.00	40.20	W	O
ATOM	5283	O	HOH W 271	18.928	13.275	29.767	1.00	52.97	W	O
ATOM	5286	O	HOH W 272	10.321	22.586	14.898	1.00	67.97	W	O
ATOM	5289	O	HOH W 273	16.890	-16.446	41.444	1.00	35.90	W	O
ATOM	5292	O	HOH W 274	4.249	-9.445	33.791	1.00	35.65	W	O
ATOM	5295	O	HOH W 275	15.844	5.952	14.465	1.00	36.89	W	O
ATOM	5298	O	HOH W 276	13.813	-22.678	27.150	1.00	43.23	W	O
ATOM	5301	O	HOH W 277	27.098	-7.831	1.776	1.00	40.66	W	O
ATOM	5304	O	HOH W 278	-5.906	22.740	35.697	1.00	36.67	W	O
ATOM	5307	O	HOH W 279	-5.273	-16.484	18.783	1.00	35.36	W	O
ATOM	5310	O	HOH W 280	-11.599	8.596	10.872	1.00	40.55	W	O
ATOM	5313	O	HOH W 281	17.212	8.689	19.402	1.00	43.11	W	O
ATOM	5316	O	HOH W 282	4.804	27.860	29.110	1.00	43.16	W	O
ATOM	5319	O	HOH W 283	5.083	13.910	18.423	1.00	42.13	W	O
ATOM	5322	O	HOH W 284	11.639	10.829	18.673	1.00	47.09	W	O
ATOM	5325	O	HOH W 285	10.959	3.360	12.881	1.00	43.06	W	O
ATOM	5328	O	HOH W 286	-1.180	-6.658	29.927	1.00	52.21	W	O
ATOM	5331	O	HOH W 287	-4.817	-13.785	18.381	1.00	38.59	W	O
ATOM	5334	O	HOH W 288	-2.046	10.931	32.923	1.00	44.39	W	O
ATOM	5337	O	HOH W 289	21.742	9.750	23.057	1.00	50.79	W	O
ATOM	5340	O	HOH W 290	17.595	6.004	16.313	1.00	37.61	W	O
ATOM	5343	O	HOH W 291	15.078	-23.825	21.692	1.00	53.24	W	O
ATOM	5346	O	HOH W 292	10.040	-2.679	36.859	1.00	38.99	W	O
ATOM	5349	O	HOH W 293	24.658	-14.439	28.467	1.00	42.29	W	O
ATOM	5352	O	HOH W 294	2.481	9.919	23.093	1.00	52.30	W	O

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ATOM   5355  O   HOH W 295     -11.544  10.199   0.951  1.00 42.96      W    O
ATOM   5358  O   HOH W 296       0.108   4.674   1.885  1.00 70.64      W    O
ATOM   5361  O   HOH W 297      -4.402 -12.590  20.752  1.00 50.92      W    O
ATOM   5364  O   HOH W 298      10.146 -23.973   6.683  1.00 53.06      W    O
ATOM   5367  O   HOH W 299      19.627 -20.265  17.138  1.00 46.12      W    O
ATOM   5370  O   HOH W 300       8.744 -22.460  11.964  1.00 54.32      W    O
ATOM   5373  O   HOH W 301      19.047  -5.541  -3.243  1.00 45.72      W    O
ATOM   5376  O   HOH W 302       3.891  -3.645  38.106  1.00 36.00      W    O
ATOM   5379  O   HOH W 303      -2.492  -8.228  26.553  1.00 43.16      W    O
ATOM   5382  O   HOH W 304      -1.716 -13.273  11.577  1.00 49.55      W    O
ATOM   5385  O   HOH W 305      10.334 -22.828  32.270  1.00 49.07      W    O
ATOM   5388  O   HOH W 306      14.641  10.583  19.949  1.00 45.35      W    O
ATOM   5391  O   HOH W 307       8.072   1.930  -8.536  1.00 52.79      W    O
ATOM   5394  O   HOH W 308      -9.064   6.600  24.242  1.00 40.71      W    O
ATOM   5397  O   HOH W 309      11.964  -1.093  38.727  1.00 41.67      W    O
ATOM   5400  O   HOH W 310      16.996   4.821   9.888  1.00 36.87      W    O
ATOM   5403  O   HOH W 311      25.026  -3.015  31.517  1.00 57.41      W    O
ATOM   5406  O   HOH W 312      -2.780  -5.682   7.256  1.00 46.09      W    O
ATOM   5409  O   HOH W 313     -18.185  11.925  34.759  1.00 40.14      W    O
ATOM   5412  O   HOH W 314      21.325   5.331  -1.232  1.00 52.23      W    O
ATOM   5415  O   HOH W 315      13.289   3.175  13.754  1.00 36.05      W    O
ATOM   5418  O   HOH W 316      20.567 -14.512  15.299  1.00 28.60      W    O
ATOM   5421  O   HOH W 317       6.126 -23.281  15.325  1.00 31.62      W    O
ATOM   5424  O   HOH W 318       7.810 -24.321  13.708  1.00 46.04      W    O
ATOM   5427  O   HOH W 319      20.804 -18.283  18.320  1.00 47.41      W    O
ATOM   5430  O   HOH W 320      22.834   4.861  -3.374  1.00 52.99      W    O
ATOM   5433  O   HOH W 321      -2.966  12.613   0.288  1.00 49.85      W    O
ATOM   5436  O   HOH W 322      -8.736   1.592  29.674  1.00 45.84      W    O
ATOM   5439  O   HOH W 323      14.053 -21.775  35.865  1.00 41.60      W    O
ATOM   5442  O   HOH W 324      -2.109 -10.636  11.844  1.00 34.80      W    O
ATOM   5445  O   HOH W 325      -0.638   6.885  14.405  1.00 48.19      W    O
ATOM   5448  O   HOH W 326      29.870  -5.489  24.392  1.00 50.31      W    O
ATOM   5451  O   HOH W 327      26.074 -16.489  27.423  1.00 61.10      W    O
ATOM   5454  O   HOH W 328     -11.632   8.051  24.014  1.00 56.95      W    O
ATOM   5457  O   HOH W 329       7.912 -20.605  14.462  1.00 44.67      W    O
ATOM   5460  O   HOH W 330      27.064 -13.871  27.167  1.00 47.91      W    O
ATOM   5463  O   HOH W 331      -2.714  11.537  -2.222  1.00 50.23      W    O
ATOM   5466  O   HOH W 332      -8.002 -16.209  18.045  1.00 34.96      W    O
ATOM   5469  O   HOH W 333      33.966  -9.397  32.778  1.00 54.54      W    O
ATOM   5472  O   HOH W 334       7.173 -25.504   7.225  1.00 53.06      W    O
ATOM   5475  O   HOH W 335      15.475 -20.063  36.278  1.00 48.34      W    O
ATOM   5478  O   HOH W 336       6.619   6.422  38.525  1.00 43.03      W    O
ATOM   5481  O   HOH W 337      -1.974   8.937  15.647  1.00 63.54      W    O
ATOM   5484  O   HOH W 338       4.790   7.735  12.579  1.00 38.37      W    O
ATOM   5487  O   HOH W 339     -13.989  17.117  22.115  1.00 51.92      W    O
ATOM   5490  O   HOH W 340     -10.024  12.553   9.238  1.00 42.11      W    O
ATOM   5493  O   HOH W 341     -13.259   7.921  26.139  1.00 42.31      W    O
ATOM   5496  O   HOH W 342      -8.537 -13.413  18.217  1.00 49.82      W    O
ATOM   5499  O   HOH W 343     -12.272  13.411  15.526  1.00 51.61      W    O
ATOM   5502  O   HOH W 344      -3.611 -14.130  22.744  1.00 45.31      W    O
ATOM   5505  O   HOH W 345      16.070  -1.755  -1.666  1.00 35.48      W    O
ATOM   5508  O   HOH W 346      11.461  20.223  27.293  1.00 52.83      W    O
ATOM   5511  O   HOH W 347       6.322  -4.058  39.620  1.00 46.01      W    O
ATOM   5514  O   HOH W 348      12.395  19.996  20.666  1.00 48.20      W    O
ATOM   5517  O   HOH W 349      11.359   6.167  -7.532  1.00 48.83      W    O
ATOM   5520  O   HOH W 350      22.764   0.708  40.869  1.00 54.11      W    O
ATOM   5523  O   HOH W 351      -5.503 -18.379  15.462  1.00 40.42      W    O
ATOM   5526  O   HOH W 352      -0.473 -15.085  12.915  1.00 68.33      W    O
ATOM   5529  O   HOH W 353      20.340 -10.912  39.803  1.00 45.04      W    O
ATOM   5532  O   HOH W 354       6.550  16.368  32.041  1.00 65.13      W    O
ATOM   5535  O   HOH W 355      -1.548 -11.778  27.806  1.00 57.13      W    O
END
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Table 2

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REMARK Written by DEALPDB Version 1.13 (06/02)
REMARK Thu Jan 23 14:56:07 2003
HEADER    ----                                    XX-XXX-XX   xxxx
COMPND    ---
REMARK   3
REMARK   3 REFINEMENT.
REMARK   3   PROGRAM     : REFMAC 5.1.25
REMARK   3   AUTHORS     : MURSHUDOV,VAGIN,DODSON
REMARK   3
REMARK   3    REFINEMENT TARGET : MAXIMUM LIKELIHOOD
REMARK   3
REMARK   3  DATA USED IN REFINEMENT.
REMARK   3   RESOLUTION RANGE HIGH (ANGSTROMS) :   1.80
REMARK   3   RESOLUTION RANGE LOW  (ANGSTROMS) :  81.65
REMARK   3   DATA CUTOFF            (SIGMA(F)) : NONE
REMARK   3   COMPLETENESS FOR RANGE        (%) :  99.77
REMARK   3   NUMBER OF REFLECTIONS             :   24820
REMARK   3
REMARK   3  FIT TO DATA USED IN REFINEMENT.
REMARK   3   CROSS-VALIDATION METHOD          : THROUGHOUT
REMARK   3   FREE R VALUE TEST SET SELECTION  : RANDOM
REMARK   3   R VALUE     (WORKING + TEST SET) : 0.18829
REMARK   3   R VALUE           (WORKING SET) :  0.18620
REMARK   3   FREE R VALUE                     :  0.22809
REMARK   3   FREE R VALUE TEST SET SIZE   (%) :  5.1
REMARK   3   FREE R VALUE TEST SET COUNT      :  1327
REMARK   3
REMARK   3  FIT IN THE HIGHEST RESOLUTION BIN.
REMARK   3   TOTAL NUMBER OF BINS USED           :      20
REMARK   3   BIN RESOLUTION RANGE HIGH           :    1.800
REMARK   3   BIN RESOLUTION RANGE LOW            :    1.847
REMARK   3   REFLECTION IN BIN     (WORKING SET) :     1749
REMARK   3   BIN R VALUE           (WORKING SET) :    0.242
REMARK   3   BIN FREE R VALUE SET COUNT          :       90
REMARK   3   BIN FREE R VALUE                    :    0.288
REMARK   3
REMARK   3  NUMBER OF NON-HYDROGEN ATOMS USED IN REFINEMENT.
REMARK   3   ALL ATOMS                 :     2507
REMARK   3
REMARK   3  B VALUES.
REMARK   3   FROM WILSON PLOT           (A**2) : NULL
REMARK   3   MEAN B VALUE      (OVERALL, A**2) :  17.218
REMARK   3   OVERALL ANISOTROPIC B VALUE.
REMARK   3    B11 (A**2) :    -0.09
REMARK   3    B22 (A**2) :     0.14
REMARK   3    B33 (A**2) :    -0.04
REMARK   3    B12 (A**2) :     0.00
REMARK   3    B13 (A**2) :    -0.02
REMARK   3    B23 (A**2) :     0.00
REMARK   3
REMARK   3  ESTIMATED OVERALL COORDINATE ERROR.
REMARK   3   ESU BASED ON R VALUE                            (A):   0.141
REMARK   3   ESU BASED ON FREE R VALUE                       (A):   0.133
REMARK   3   ESU BASED ON MAXIMUM LIKELIHOOD                 (A):   0.082
REMARK   3   ESU FOR B VALUES BASED ON MAXIMUM LIKELIHOOD (A**2):   2.620
REMARK   3
REMARK   3 CORRELATION COEFFICIENTS.
REMARK   3   CORRELATION COEFFICIENT FO-FC      :   0.948
REMARK   3   CORRELATION COEFFICIENT FO-FC FREE :   0.929
REMARK   3
REMARK   3  RMS DEVIATIONS FROM IDEAL VALUES        COUNT    RMS    WEIGHT
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REMARK   3   BOND LENGTHS REFINED ATOMS        (A):  2310 ; 0.010 ; 0.022
REMARK   3   BOND LENGTHS OTHERS               (A):  2097 ; 0.002 ; 0.020
REMARK   3   BOND ANGLES REFINED ATOMS   (DEGREES):  3134 ; 1.372 ; 1.981
REMARK   3   BOND ANGLES OTHERS          (DEGREES):  4890 ; 0.790 ; 3.000
REMARK   3   TORSION ANGLES, PERIOD 1    (DEGREES):   272 ; 5.281 ; 5.000
REMARK   3   CHIRAL-CENTER RESTRAINTS       (A**3):   344 ; 0.076 ; 0.200
REMARK   3   GENERAL PLANES REFINED ATOMS      (A):  2489 ; 0.005 ; 0.020
REMARK   3   GENERAL PLANES OTHERS             (A):   465 ; 0.002 ; 0.020
REMARK   3   NON-BONDED CONTACTS REFINED ATOMS (A):   475 ; 0.205 ; 0.200
REMARK   3   NON-BONDED CONTACTS OTHERS        (A):  2364 ; 0.223 ; 0.200
REMARK   3   NON-BONDED TORSION OTHERS         (A):  1222 ; 0.081 ; 0.200
REMARK   3   H-BOND (X...Y) REFINED ATOMS      (A):   147 ; 0.162 ; 0.200
REMARK   3   SYMMETRY VDW REFINED ATOMS        (A):    21 ; 0.168 ; 0.200
REMARK   3   SYMMETRY VDW OTHERS               (A):    86 ; 0.250 ; 0.200
REMARK   3   SYMMETRY H-BOND REFINED ATOMS     (A):    14 ; 0.111 ; 0.200
REMARK   3
REMARK   3  ISOTROPIC THERMAL FACTOR RESTRAINTS.     COUNT   RMS    WEIGHT
REMARK   3   MAIN-CHAIN BOND REFINED ATOMS  (A**2):  1365 ; 0.818 ; 1.500
REMARK   3   MAIN-CHAIN ANGLE REFINED ATOMS (A**2):  2224 ; 1.568 ; 2.000
REMARK   3   SIDE-CHAIN BOND REFINED ATOMS  (A**2):   945 ; 2.206 ; 3.000
REMARK   3   SIDE-CHAIN ANGLE REFINED ATOMS (A**2):   910 ; 3.668 ; 4.500
REMARK   3
REMARK   3  NCS RESTRAINTS STATISTICS
REMARK   3   NUMBER OF NCS GROUPS : NULL
REMARK   3
REMARK   3
REMARK   3  TLS DETAILS
REMARK   3   NUMBER OF TLS GROUPS  :    1
REMARK   3
REMARK   3   TLS GROUP :     1
REMARK   3    NUMBER OF COMPONENTS GROUP :    1
REMARK   3    COMPONENTS        C SSSEQI   TO  C SSSEQI
REMARK   3    RESIDUE RANGE :   A   419        A   691
REMARK   3    ORIGIN FOR THE GROUP (A):   6.9620   1.7680  19.1340
REMARK   3    T TENSOR
REMARK   3      T11:   0.0048 T22:   0.0352
REMARK   3      T33:   0.0580 T12:  -0.0119
REMARK   3      T13:  -0.0081 T23:   0.0084
REMARK   3    L TENSOR
REMARK   3      L11:   0.3962 L22:   0.3784
REMARK   3      L33:   0.2902 L12:  -0.1647
REMARK   3      L13:   0.0731 L23:   0.0592
REMARK   3    S TENSOR
REMARK   3      S11:  -0.0145 S12:   0.0246 S13:   0.0170
REMARK   3      S21:   0.0077 S22:   0.0410 S23:   0.0381
REMARK   3      S31:  -0.0159 S32:   0.0355 S33:  -0.0265
REMARK   3
REMARK   3
REMARK   3  BULK SOLVENT MODELLING.
REMARK   3   METHOD USED : BABINET MODEL WITH MASK
REMARK   3   PARAMETERS FOR MASK CALCULATION
REMARK   3   VDW PROBE RADIUS   :   1.40
REMARK   3   ION PROBE RADIUS   :   0.80
REMARK   3   SHRINKAGE RADIUS   :   0.80
REMARK   3
REMARK   3  OTHER REFINEMENT REMARKS:
REMARK   3  HYDROGENS HAVE BEEN ADDED IN THE RIDING POSITIONS
REMARK   3
CRYST1   37.316   46.978   81.109  90.00  92.83  90.00 P 1 21 1
SCALE1      0.026798  0.000000  0.001323        0.00000
SCALE2      0.000000  0.021287  0.000000        0.00000
SCALE3      0.000000  0.000000  0.012344        0.00000
ATOM      1  N   MET A 419     -17.724  15.274  26.545  1.00 41.92      A    N
ATOM      3  CA  MET A 419     -16.798  15.014  25.404  1.00 41.87      A    C
ATOM      5  CB  MET A 419     -17.513  15.303  24.075  1.00 42.37      A    C
ATOM      8  CG  MET A 419     -18.905  14.692  23.955  1.00 44.21      A    C
ATOM     11  SD  MET A 419     -18.872  12.884  23.783  1.00 48.64      A    S
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ATOM     12  CE  MET A 419     -19.036  12.354  25.521  1.00 47.82      A    C
ATOM     16  C   MET A 419     -15.527  15.875  25.505  1.00 40.85      A    C
ATOM     17  O   MET A 419     -14.857  16.115  24.495  1.00 41.39      A    O
ATOM     20  N   ILE A 420     -15.200  16.322  26.719  1.00 39.21      A    N
ATOM     22  CA  ILE A 420     -14.050  17.208  26.982  1.00 37.79      A    C
ATOM     24  CB  ILE A 420     -12.697  16.519  26.689  1.00 37.82      A    C
ATOM     26  CG1 ILE A 420     -12.557  15.240  27.512  1.00 38.41      A    C
ATOM     29  CD1 ILE A 420     -11.209  14.556  27.348  1.00 38.81      A    C
ATOM     33  CG2 ILE A 420     -11.539  17.494  26.996  1.00 37.64      A    C
ATOM     37  C   ILE A 420     -14.081  18.526  26.218  1.00 36.12      A    C
ATOM     38  O   ILE A 420     -13.850  18.561  25.013  1.00 36.25      A    O
ATOM     39  N   ALA A 421     -14.316  19.613  26.935  1.00 34.13      A    N
ATOM     41  CA  ALA A 421     -14.207  20.936  26.356  1.00 32.57      A    C
ATOM     43  CB  ALA A 421     -15.126  21.909  27.076  1.00 32.58      A    C
ATOM     47  C   ALA A 421     -12.762  21.394  26.457  1.00 31.11      A    C
ATOM     48  O   ALA A 421     -12.009  20.935  27.315  1.00 30.48      A    O
ATOM     49  N   ARG A 422     -12.385  22.305  25.572  1.00 29.35      A    N
ATOM     51  CA  ARG A 422     -11.069  22.917  25.610  1.00 28.21      A    C
ATOM     53  CB  ARG A 422     -10.957  23.974  24.506  1.00 28.08      A    C
ATOM     56  CG  ARG A 422      -9.542  24.501  24.279  1.00 27.30      A    C
ATOM     59  CD  ARG A 422      -9.471  25.640  23.289  1.00 25.94      A    C
ATOM     62  NE  ARG A 422     -10.069  25.288  22.005  1.00 25.59      A    N
ATOM     64  CZ  ARG A 422      -9.474  24.572  21.057  1.00 24.52      A    C
ATOM     65  NH1 ARG A 422      -8.241  24.095  21.225  1.00 22.64      A    N
ATOM     68  NH2 ARG A 422     -10.124  24.320  19.932  1.00 24.29      A    N
ATOM     71  C   ARG A 422     -10.773  23.535  26.985  1.00 27.22      A    C
ATOM     72  O   ARG A 422      -9.632  23.519  27.435  1.00 26.74      A    O
ATOM     73  N   GLU A 423     -11.808  24.051  27.652  1.00 26.08      A    N
ATOM     75  CA  GLU A 423     -11.674  24.666  28.979  1.00 25.78      A    C
ATOM     77  CB  GLU A 423     -13.012  25.237  29.474  1.00 26.29      A    C
ATOM     80  CG  GLU A 423     -13.662  26.233  28.552  1.00 28.01      A    C
ATOM     83  CD  GLU A 423     -14.629  25.584  27.583  1.00 29.62      A    C
ATOM     84  OE1 GLU A 423     -14.183  25.287  26.450  1.00 28.40      A    O
ATOM     85  OE2 GLU A 423     -15.823  25.382  27.960  1.00 30.82      A    O
ATOM     86  C   GLU A 423     -11.224  23.675  30.040  1.00 24.55      A    C
ATOM     87  O   GLU A 423     -10.636  24.070  31.034  1.00 24.25      A    O
ATOM     88  N   ASP A 424     -11.550  22.401  29.843  1.00 23.65      A    N
ATOM     90  CA  ASP A 424     -11.151  21.351  30.778  1.00 23.18      A    C
ATOM     92  CB  ASP A 424     -11.925  20.056  30.503  1.00 23.13      A    C
ATOM     95  CG  ASP A 424     -13.436  20.219  30.670  1.00 25.17      A    C
ATOM     96  OD1 ASP A 424     -13.848  21.127  31.427  1.00 26.20      A    O
ATOM     97  OD2 ASP A 424     -14.276  19.481  30.095  1.00 26.16      A    O
ATOM     98  C   ASP A 424      -9.639  21.067  30.742  1.00 22.42      A    C
ATOM     99  O   ASP A 424      -9.148  20.360  31.606  1.00 21.99      A    O
ATOM    100  N   VAL A 425      -8.920  21.606  29.752  1.00 21.44      A    N
ATOM    102  CA  VAL A 425      -7.488  21.342  29.592  1.00 21.23      A    C
ATOM    104  CB  VAL A 425      -7.184  20.639  28.249  1.00 21.09      A    C
ATOM    106  CG1 VAL A 425      -5.678  20.393  28.092  1.00 21.37      A    C
ATOM    110  CG2 VAL A 425      -7.963  19.337  28.133  1.00 20.93      A    C
ATOM    114  C   VAL A 425      -6.715  22.641  29.649  1.00 21.24      A    C
ATOM    115  O   VAL A 425      -6.957  23.541  28.836  1.00 21.03      A    O
ATOM    116  N   VAL A 426      -5.824  22.742  30.631  1.00 20.75      A    N
ATOM    118  CA  VAL A 426      -4.965  23.894  30.830  1.00 21.32      A    C
ATOM    120  CB  VAL A 426      -4.992  24.367  32.300  1.00 21.30      A    C
ATOM    122  CG1 VAL A 426      -4.044  25.545  32.514  1.00 22.52      A    C
ATOM    126  CG2 VAL A 426      -6.415  24.743  32.718  1.00 21.78      A    C
ATOM    130  C   VAL A 426      -3.522  23.530  30.466  1.00 21.27      A    C
ATOM    131  O   VAL A 426      -2.931  22.621  31.046  1.00 20.65      A    O
ATOM    132  N   LEU A 427      -2.960  24.253  29.509  1.00 21.37      A    N
ATOM    134  CA  LEU A 427      -1.585  24.024  29.079  1.00 21.38      A    C
ATOM    136  CB  LEU A 427      -1.413  24.387  27.593  1.00 21.39      A    C
ATOM    139  CG  LEU A 427      -2.428  23.797  26.603  1.00 21.09      A    C
ATOM    141  CD1 LEU A 427      -2.214  24.341  25.191  1.00 21.00      A    C
ATOM    145  CD2 LEU A 427      -2.399  22.267  26.592  1.00 20.75      A    C
ATOM    149  C   LEU A 427      -0.626  24.841  29.931  1.00 22.15      A    C
ATOM    150  O   LEU A 427      -0.819  26.043  30.102  1.00 21.62      A    O
ATOM    151  N   ASN A 428       0.413  24.189  30.448  1.00 22.43      A    N
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ATOM    153  CA  ASN A 428       1.416  24.834  31.311  1.00 23.45      A    C
ATOM    155  CB  ASN A 428       1.710  23.923  32.508  1.00 23.76      A    C
ATOM    158  CG  ASN A 428       0.458  23.579  33.293  1.00 26.13      A    C
ATOM    159  OD1 ASN A 428       0.301  22.454  33.774  1.00 30.61      A    O
ATOM    160  ND2 ASN A 428      -0.455  24.536  33.400  1.00 28.03      A    N
ATOM    163  C   ASN A 428       2.728  25.192  30.611  1.00 23.29      A    C
ATOM    164  O   ASN A 428       3.316  26.231  30.907  1.00 23.11      A    O
ATOM    165  N   ARG A 429       3.217  24.316  29.732  1.00 23.23      A    N
ATOM    167  CA  ARG A 429       4.438  24.593  28.965  1.00 23.80      A    C
ATOM    169  CB  ARG A 429       5.678  24.419  29.846  1.00 24.47      A    C
ATOM    172  CG  ARG A 429       5.945  22.999  30.298  1.00 26.49      A    C
ATOM    175  CD  ARG A 429       7.254  22.845  31.078  1.00 30.54      A    C
ATOM    178  NE  ARG A 429       7.866  21.544  30.824  1.00 34.08      A    N
ATOM    180  CZ  ARG A 429       8.873  21.315  29.980  1.00 35.96      A    C
ATOM    181  NH1 ARG A 429       9.438  22.308  29.290  1.00 36.94      A    N
ATOM    184  NH2 ARG A 429       9.330  20.077  29.838  1.00 36.82      A    N
ATOM    187  C   ARG A 429       4.596  23.731  27.715  1.00 23.63      A    C
ATOM    188  O   ARG A 429       3.847  22.785  27.506  1.00 22.57      A    O
ATOM    189  N   ILE A 430       5.592  24.053  26.895  1.00 23.59      A    N
ATOM    191  CA  ILE A 430       5.901  23.258  25.711  1.00 24.18      A    C
ATOM    193  CB  ILE A 430       6.382  24.161  24.535  1.00 24.28      A    C
ATOM    195  CG1 ILE A 430       5.211  25.021  24.046  1.00 24.59      A    C
ATOM    198  CD1 ILE A 430       5.513  25.900  22.844  1.00 23.92      A    C
ATOM    202  CG2 ILE A 430       6.967  23.305  23.398  1.00 24.51      A    C
ATOM    206  C   ILE A 430       6.914  22.169  26.036  1.00 25.15      A    C
ATOM    207  O   ILE A 430       7.978  22.435  26.594  1.00 25.52      A    O
ATOM    208  N   LEU A 431       6.555  20.940  25.683  1.00 26.06      A    N
ATOM    210  CA  LEU A 431       7.351  19.745  25.935  1.00 27.29      A    C
ATOM    212  CB  LEU A 431       6.411  18.533  25.929  1.00 27.83      A    C
ATOM    215  CG  LEU A 431       6.627  17.314  26.814  1.00 29.05      A    C
ATOM    217  CD1 LEU A 431       7.002  17.675  28.242  1.00 29.90      A    C
ATOM    221  CD2 LEU A 431       5.346  16.505  26.789  1.00 29.38      A    C
ATOM    225  C   LEU A 431       8.423  19.572  24.863  1.00 28.18      A    C
ATOM    226  O   LEU A 431       9.582  19.243  25.149  1.00 28.38      A    O
ATOM    227  N   GLY A 432       8.024  19.793  23.620  1.00 28.92      A    N
ATOM    229  CA  GLY A 432       8.932  19.691  22.500  1.00 29.66      A    C
ATOM    232  C   GLY A 432       8.267  19.963  21.166  1.00 30.32      A    C
ATOM    233  O   GLY A 432       7.040  20.023  21.065  1.00 29.86      A    O
ATOM    234  N   GLU A 433       9.096  20.144  20.144  1.00 31.32      A    N
ATOM    236  CA  GLU A 433       8.636  20.260  18.767  1.00 32.42      A    C
ATOM    238  CB  GLU A 433       9:600  21.120  17.946  1.00 33.03      A    C
ATOM    241  CG  GLU A 433       9.426  21.056  16.433  1.00 35.97      A    C
ATOM    244  CD  GLU A 433       8.136  21.696  15.966  1.00 39.52      A    C
ATOM    245  OE1 GLU A 433       7.078  21.062  16.142  1.00 41.45      A    O
ATOM    246  OE2 GLU A 433       8.178  22.828  15.417  1.00 43.45      A    O
ATOM    247  C   GLU A 433       8.559  18.853  18.200  1.00 32.62      A    C
ATOM    248  O   GLU A 433       9.584  18.218  17.959  1.00 33.07      A    O
ATOM    249  N   GLY A 434       7.341  18.364  18.027  1.00 32.46      A    N
ATOM    251  CA  GLY A 434       7.110  17.080  17.411  1.00 32.53      A    C
ATOM    254  C   GLY A 434       6.926  17.141  15.904  1.00 32.66      A    C
ATOM    255  O   GLY A 434       7.033  18.193  15.266  1.00 32.19      A    O
ATOM    256  N   PHE A 435       6.619  15.974  15.353  1.00 32.83      A    N
ATOM    258  CA  PHE A 435       6.413  15.765  13.926  1.00 32.68      A    C
ATOM    260  CB  PHE A 435       6.032  14.294  13.703  1.00 33.30      A    C
ATOM    263  CG  PHE A 435       6.016  13.890  12.267  1.00 35.29      A    C
ATOM    264  CD1 PHE A 435       7.202  13.628  11.601  1.00 37.64      A    C
ATOM    266  CE1 PHE A 435       7.197  13.260  10.263  1.00 38.62      A    C
ATOM    268  CZ  PHE A 435       6.000  13.162   9.582  1.00 38.93      A    C
ATOM    270  CE2 PHE A 435       4.807  13.434  10.236  1.00 38.98      A    C
ATOM    272  CD2 PHE A 435       4.821  13.794  11.575  1.00 36.99      A    C
ATOM    274  C   PHE A 435       5.330  16.662  13.319  1.00 31.77      A    C
ATOM    275  O   PHE A 435       5.533  17.269  12.262  1.00 31.44      A    O
ATOM    276  N   PHE A 436       4.178  16.734  13.982  1.00 30.64      A    N
ATOM    278  CA  PHE A 436       3.030  17.476  13.465  1.00 29.83      A    C
ATOM    280  CB  PHE A 436       1.716  16.792  13.880  1.00 30.65      A    C
ATOM    283  CG  PHE A 436       1.425  15.511  13.114  1.00 33.59      A    C
ATOM    284  CD1 PHE A 436       0.993  15.554  11.791  1.00 36.89      A    C
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ATOM	286	CE1	PHE	A	436	0.731	14.368	11.076	1.00	38.35	A	C
ATOM	288	CZ	PHE	A	436	0.917	13.136	11.692	1.00	38.06	A	C
ATOM	290	CE2	PHE	A	436	1.354	13.086	13.006	1.00	37.74	A	C
ATOM	292	CD2	PHE	A	436	1.608	14.268	13.709	1.00	36.81	A	C
ATOM	294	C	PHE	A	436	3.036	18.949	13.904	1.00	27.92	A	C
ATOM	295	O	PHE	A	436	2.435	19.783	13.242	1.00	26.90	A	O
ATOM	296	N	GLY	A	437	3.713	19.242	15.021	1.00	25.85	A	N
ATOM	298	CA	GLY	A	437	3.773	20.582	15.598	1.00	24.35	A	C
ATOM	301	C	GLY	A	437	4.152	20.555	17.076	1.00	23.03	A	C
ATOM	302	O	GLY	A	437	4.635	19.549	17.596	1.00	22.52	A	O
ATOM	303	N	GLU	A	438	3.912	21.660	17.774	1.00	21.56	A	N
ATOM	305	CA	GLU	A	438	4.295	21.761	19.176	1.00	20.35	A	C
ATOM	307	CB	GLU	A	438	4.114	23.191	19.694	1.00	20.82	A	C
ATOM	310	CG	GLU	A	438	4.921	24.235	18.922	1.00	23.31	A	C
ATOM	313	CD	GLU	A	438	6.325	24.443	19.459	1.00	26.75	A	C
ATOM	314	OE1	GLU	A	438	6.960	23.454	19.896	1.00	24.49	A	O
ATOM	315	OE2	GLU	A	438	6.792	25.611	19.446	1.00	29.56	A	O
ATOM	316	C	GLU	A	438	3.473	20.781	20.016	1.00	18.49	A	C
ATOM	317	O	GLU	A	438	2.306	20.552	19.744	1.00	17.45	A	O
ATOM	318	N	VAL	A	439	4.124	20.199	21.017	1.00	17.29	A	N
ATOM	320	CA	VAL	A	439	3.498	19.315	21.986	1.00	16.28	A	C
ATOM	322	CB	VAL	A	439	4.183	17.933	22.024	1.00	16.57	A	C
ATOM	324	CG1	VAL	A	439	3.516	17.038	23.065	1.00	17.25	A	C
ATOM	328	CG2	VAL	A	439	4.141	17.301	20.643	1.00	16.55	A	C
ATOM	332	C	VAL	A	439	3.623	19.974	23.350	1.00	15.68	A	C
ATOM	333	O	VAL	A	439	4.705	20.380	23.732	1.00	14.39	A	O
ATOM	334	N	TYR	A	440	2.508	20.084	24.068	1.00	14.79	A	N
ATOM	336	CA	TYR	A	440	2.447	20.789	25.345	1.00	14.71	A	C
ATOM	338	CB	TYR	A	440	1.269	21.749	25.334	1.00	14.65	A	C
ATOM	341	CG	TYR	A	440	1.348	22.842	24.301	1.00	15.25	A	C
ATOM	342	CD1	TYR	A	440	1.809	24.110	24.639	1.00	16.36	A	C
ATOM	344	CE1	TYR	A	440	1.860	25.135	23.691	1.00	16.17	A	C
ATOM	346	CZ	TYR	A	440	1.436	24.895	22.395	1.00	18.28	A	C
ATOM	347	OH	TYR	A	440	1.490	25.905	21.453	1.00	20.25	A	O
ATOM	349	CE2	TYR	A	440	0.967	23.644	22.038	1.00	16.17	A	C
ATOM	351	CD2	TYR	A	440	0.916	22.630	22.994	1.00	14.61	A	C
ATOM	353	C	TYR	A	440	2.228	19.817	26.479	1.00	15.34	A	C
ATOM	354	O	TYR	A	440	1.608	18.765	26.270	1.00	15.00	A	O
ATOM	355	N	GLU	A	441	2.723	20.168	27.669	1.00	15.04	A	N
ATOM	357	CA	GLU	A	441	2.340	19.514	28.921	1.00	16.43	A	C
ATOM	359	CB	GLU	A	441	3.513	19.470	29.916	1.00	17.43	A	C
ATOM	362	CG	GLU	A	441	3.244	18.575	31.117	1.00	21.96	A	C
ATOM	365	CD	GLU	A	441	4.331	18.631	32.173	1.00	28.06	A	C
ATOM	366	OE1	GLU	A	441	5.533	18.478	31.828	1.00	31.85	A	O
ATOM	367	OE2	GLU	A	441	3.975	18.829	33.361	1.00	32.28	A	O
ATOM	368	C	GLU	A	441	1.196	20.317	29.514	1.00	15.91	A	C
ATOM	369	O	GLU	A	441	1.205	21.549	29.457	1.00	15.73	A	O
ATOM	370	N	GLY	A	442	0.214	19.627	30.074	1.00	15.38	A	N
ATOM	372	CA	GLY	A	442	-0.938	20.279	30.679	1.00	15.56	A	C
ATOM	375	C	GLY	A	442	-1.686	19.408	31.671	1.00	15.46	A	C
ATOM	376	O	GLY	A	442	-1.266	18.295	31.998	1.00	14.91	A	O
ATOM	377	N	VAL	A	443	-2.799	19.937	32.159	1.00	15.90	A	N
ATOM	379	CA	VAL	A	443	-3.655	19.250	33.120	1.00	15.95	A	C
ATOM	381	CB	VAL	A	443	-3.585	19.926	34.515	1.00	15.99	A	C
ATOM	383	CG1	VAL	A	443	-4.535	19.256	35.486	1.00	16.92	A	C
ATOM	387	CG2	VAL	A	443	-2.159	19.901	35.054	1.00	16.66	A	C
ATOM	391	C	VAL	A	443	-5.088	19.235	32.606	1.00	16.11	A	C
ATOM	392	O	VAL	A	443	-5.677	20.280	32.328	1.00	16.39	A	O
ATOM	393	N	TYR	A	444	-5.645	18.039	32.474	1.00	16.07	A	N
ATOM	395	CA	TYR	A	444	-7.053	17.833	32.189	1.00	16.30	A	C
ATOM	397	CB	TYR	A	444	-7.210	16.696	31.179	1.00	16.55	A	C
ATOM	400	CG	TYR	A	444	-8.608	16.106	31.085	1.00	16.49	A	C
ATOM	401	CD1	TYR	A	444	-9.735	16.925	30.992	1.00	17.40	A	C
ATOM	403	CE1	TYR	A	444	-11.002	16.376	30.907	1.00	18.98	A	C
ATOM	405	CZ	TYR	A	444	-11.159	15.013	30.900	1.00	19.67	A	C
ATOM	406	OH	TYR	A	444	-12.417	14.454	30.818	1.00	22.12	A	O
ATOM	408	CE2	TYR	A	444	-10.066	14.189	30.992	1.00	18.71	A	C

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ATOM    410  CD2 TYR A 444      -8.801  14.737  31.070  1.00 18.30      A    C
ATOM    412  C   TYR A 444      -7.828  17.530  33.495  1.00 16.91      A    C
ATOM    413  O   TYR A 444      -7.500  16.593  34.223  1.00 16.06      A    O
ATOM    414  N   THR A 445      -8.845  18.338  33.779  1.00 17.53      A    N
ATOM    416  CA  THR A 445      -9.703  18.146  34.944  1.00 18.31      A    C
ATOM    418  CB  THR A 445      -9.911  19.475  35.684  1.00 18.17      A    C
ATOM    420  OG1 THR A 445      -8.651  20.045  36.030  1.00 19.23      A    O
ATOM    422  CG2 THR A 445     -10.578  19.262  37.044  1.00 18.29      A    C
ATOM    426  C   THR A 445     -11.032  17.632  34.430  1.00 19.18      A    C
ATOM    427  O   THR A 445     -11.702  18.345  33.694  1.00 19.17      A    O
ATOM    428  N   ASN A 446     -11.402  16.403  34.791  1.00 19.93      A    N
ATOM    430  CA  ASN A 446     -12.665  15.825  34.351  1.00 21.09      A    C
ATOM    432  CB  ASN A 446     -12.617  14.266  34.318  1.00 21.05      A    C
ATOM    435  CG  ASN A 446     -12.502  13.602  35.704  1.00 21.28      A    C
ATOM    436  OD1 ASN A 446     -12.158  12.407  35.796  1.00 22.39      A    O
ATOM    437  ND2 ASN A 446     -12.778  14.345  36.766  1.00 18.07      A    N
ATOM    440  C   ASN A 446     -13.831  16.414  35.163  1.00 22.07      A    C
ATOM    441  O   ASN A 446     -13.646  17.396  35.907  1.00 22.06      A    O
ATOM    442  N   HIS A 447     -15.025  15.861  34.999  1.00 23.22      A    N
ATOM    444  CA  HIS A 447     -16.215  16.446  35.621  1.00 24.56      A    C
ATOM    446  CB  HIS A 447     -17.479  16.009  34.878  1.00 25.52      A    C
ATOM    449  CG  HIS A 447     -17.560  16.535  33.474  1.00 28.90      A    C
ATOM    450  ND1 HIS A 447     -17.485  17.879  33.177  1.00 32.01      A    N
ATOM    452  CE1 HIS A 447     -17.581  18.047  31.869  1.00 32.90      A    C
ATOM    454  NE2 HIS A 447     -17.712  16.859  31.306  1.00 33.63      A    N
ATOM    456  CD2 HIS A 447     -17.703  15.896  32.289  1.00 32.36      A    C
ATOM    458  C   HIS A 447     -16.323  16.121  37.113  1.00 24.17      A    C
ATOM    459  O   HIS A 447     -17.141  16.715  37.819  1.00 24.60      A    O
ATOM    460  N   LYS A 448     -15.513  15.168  37.575  1.00 23.56      A    N
ATOM    462  CA  LYS A 448     -15.440  14.802  38.994  1.00 23.13      A    C
ATOM    464  CB  LYS A 448     -15.188  13.302  39.137  1.00 23.02      A    C
ATOM    467  CG  LYS A 448     -16.354  12.461  38.679  1.00 23.56      A    C
ATOM    470  CD  LYS A 448     -15.916  11.043  38.364  1.00 24.68      A    C
ATOM    473  CE  LYS A 448     -17.090  10.180  37.907  1.00 25.53      A    C
ATOM    476  NZ  LYS A 448     -16.689   8.742  37.931  1.00 23.92      A    N
ATOM    480  C   LYS A 448     -14.353  15.561  39.758  1.00 22.72      A    C
ATOM    481  O   LYS A 448     -14.197  15.369  40.974  1.00 23.18      A    O
ATOM    482  N   GLY A 449     -13.606  16.401  39.048  1.00 21.47      A    N
ATOM    484  CA  GLY A 449     -12.580  17.234  39.648  1.00 21.53      A    C
ATOM    487  C   GLY A 449     -11.237  16.542  39.729  1.00 21.19      A    C
ATOM    488  O   GLY A 449     -10.319  17.047  40.366  1.00 20.74      A    O
ATOM    489  N   GLU A 450     -11.127  15.386  39.080  1.00 20.98      A    N
ATOM    491  CA  GLU A 450      -9.879  14.630  39.054  1.00 21.35      A    C
ATOM    493  CB  GLU A 450     -10.150  13.172  38.691  1.00 21.63      A    C
ATOM    496  CG  GLU A 450     -11.186  12.486  39.565  1.00 23.33      A    C
ATOM    499  CD  GLU A 450     -11.347  11.024  39.214  1.00 26.08      A    C
ATOM    500  OE1 GLU A 450     -10.821  10.178  39.963  1.00 26.94      A    O
ATOM    501  OE2 GLU A 450     -12.024  10.726  38.201  1.00 28.51      A    O
ATOM    502  C   GLU A 450      -8.955  15.232  38.019  1.00 21.24      A    C
ATOM    503  O   GLU A 450      -9.376  15.478  36.902  1.00 20.28      A    O
ATOM    504  N   LYS A 451      -7.691  15.436  38.388  1.00 21.76      A    N
ATOM    506  CA  LYS A 451      -6.694  16.059  37.507  1.00 21.92      A    C
ATOM    508  CB  LYS A 451      -5.963  17.166  38.254  1.00 22.51      A    C
ATOM    511  CG  LYS A 451      -6.919  18.230  38.784  1.00 23.99      A    C
ATOM    514  CD  LYS A 451      -6.239  19.546  39.068  1.00 26.30      A    C
ATOM    517  CE  LYS A 451      -7.250  20.582  39.558  1.00 27.02      A    C
ATOM    520  NZ  LYS A 451      -7.947  21.286  38.459  1.00 26.84      A    N
ATOM    524  C   LYS A 451      -5.707  15.026  36.956  1.00 21.70      A    C
ATOM    525  O   LYS A 451      -5.111  14.249  37.707  1.00 22.12      A    O
ATOM    526  N   ILE A 452      -5.586  15.005  35.633  1.00 20.88      A    N
ATOM    528  CA  ILE A 452      -4.729  14.074  34.923  1.00 20.89      A    C
ATOM    530  CB  ILE A 452      -5.587  13.104  34.051  1.00 21.84      A    C
ATOM    532  CG1 ILE A 452      -4.773  11.937  33.512  1.00 24.27      A    C
ATOM    535  CD1 ILE A 452      -4.557  10.839  34.539  1.00 27.03      A    C
ATOM    539  CG2 ILE A 452      -6.222  13.783  32.894  1.00 23.92      A    C
ATOM    543  C   ILE A 452      -3.743  14.883  34.086  1.00 19.23      A    C
ATOM    544  O   ILE A 452      -4.127  15.801  33.366  1.00 17.19      A    O
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ATOM	545	N	ASN	A	453	-2.468	14.561	34.227	1.00	18.03	A	N
ATOM	547	CA	ASN	A	453	-1.427	15.173	33.421	1.00	16.96	A	C
ATOM	549	CB	ASN	A	453	-0.039	14.893	34.019	1.00	17.63	A	C
ATOM	552	CG	ASN	A	453	0.144	15.546	35.375	1.00	19.82	A	C
ATOM	553	OD1	ASN	A	453	-0.283	16.675	35.581	1.00	20.59	A	O
ATOM	554	ND2	ASN	A	453	0.782	14.835	36.307	1.00	22.47	A	N
ATOM	557	C	ASN	A	453	-1.537	14.640	32.002	1.00	15.39	A	C
ATOM	558	O	ASN	A	453	-1.741	13.432	31.792	1.00	13.98	A	O
ATOM	559	N	VAL	A	454	-1.442	15.553	31.040	1.00	13.24	A	N
ATOM	561	CA	VAL	A	454	-1.609	15.230	29.630	1.00	12.28	A	C
ATOM	563	CB	VAL	A	454	-3.001	15.671	29.107	1.00	11.15	A	C
ATOM	565	CG1	VAL	A	454	-4.107	14.882	29.798	1.00	11.44	A	C
ATOM	569	CG2	VAL	A	454	-3.210	17.193	29.273	1.00	10.74	A	C
ATOM	573	C	VAL	A	454	-0.515	15.843	28.752	1.00	12.12	A	C
ATOM	574	O	VAL	A	454	0.128	16.843	29.123	1.00	11.68	A	O
ATOM	575	N	ALA	A	455	-0.276	15.196	27.615	1.00	11.65	A	N
ATOM	577	CA	ALA	A	455	0.496	15.770	26.521	1.00	11.60	A	C
ATOM	579	CB	ALA	A	455	1.493	14.785	25.979	1.00	12.08	A	C
ATOM	583	C	ALA	A	455	-0.511	16.142	25.435	1.00	12.46	A	C
ATOM	584	O	ALA	A	455	-1.331	15.327	25.055	1.00	12.88	A	O
ATOM	585	N	VAL	A	456	-0.459	17.384	24.968	1.00	11.82	A	N
ATOM	587	CA	VAL	A	456	-1.368	17.858	23.960	1.00	12.46	A	C
ATOM	589	CB	VAL	A	456	-2.073	19.125	24.456	1.00	12.62	A	C
ATOM	591	CG1	VAL	A	456	-2.956	19.704	23.364	1.00	13.07	A	C
ATOM	595	CG2	VAL	A	456	-2.883	18.786	25.679	1.00	12.74	A	C
ATOM	599	C	VAL	A	456	-0.622	18.148	22.668	1.00	13.13	A	C
ATOM	600	O	VAL	A	456	0.252	19.006	22.631	1.00	12.69	A	O
ATOM	601	N	LYS	A	457	-0.958	17.415	21.616	1.00	13.43	A	N
ATOM	603	CA	LYS	A	457	-0.324	17.577	20.322	1.00	14.66	A	C
ATOM	605	CB	LYS	A	457	-0.214	16.220	19.615	1.00	15.55	A	C
ATOM	608	CG	LYS	A	457	0.694	15.217	20.350	1.00	18.42	A	C
ATOM	611	CD	LYS	A	457	0.840	13.874	19.626	1.00	22.96	A	C
ATOM	614	CE	LYS	A	457	1.221	14.008	18.151	1.00	26.16	A	C
ATOM	617	NZ	LYS	A	457	1.738	12.702	17.608	1.00	29.52	A	N
ATOM	621	C	LYS	A	457	-1.123	18.569	19.480	1.00	14.79	A	C
ATOM	622	O	LYS	A	457	-2.350	18.553	19.483	1.00	14.94	A	O
ATOM	623	N	THR	A	458	-0.421	19.452	18.787	1.00	16.01	A	N
ATOM	625	CA	THR	A	458	-1.056	20.426	17.902	1.00	17.14	A	C
ATOM	627	CB	THR	A	458	-0.974	21.856	18.470	1.00	17.23	A	C
ATOM	629	OG1	THR	A	458	0.390	22.295	18.492	1.00	16.75	A	O
ATOM	631	CG2	THR	A	458	-1.437	21.907	19.927	1.00	18.01	A	C
ATOM	635	C	THR	A	458	-0.380	20.398	16.541	1.00	18.40	A	C
ATOM	636	O	THR	A	458	0.705	19.846	16.397	1.00	18.01	A	O
ATOM	637	N	CYS	A	459	-1.032	21.017	15.561	1.00	20.44	A	N
ATOM	639	CA	CYS	A	459	-0.512	21.123	14.195	1.00	22.30	A	C
ATOM	641	CB	CYS	A	459	-1.643	20.944	13.189	1.00	22.75	A	C
ATOM	644	SG	CYS	A	459	-2.097	19.219	12.971	1.00	27.79	A	S
ATOM	645	C	CYS	A	459	0.174	22.470	13.959	1.00	22.93	A	C
ATOM	646	O	CYS	A	459	-0.344	23.509	14.347	1.00	22.16	A	O
ATOM	647	N	LYS	A	460	1.347	22.426	13.337	1.00	24.00	A	N
ATOM	649	CA	LYS	A	460	2.082	23.624	12.970	1.00	25.15	A	C
ATOM	651	CB	LYS	A	460	3.487	23.276	12.461	1.00	25.42	A	C
ATOM	654	CG	LYS	A	460	3.540	22.407	11.195	1.00	27.60	A	C
ATOM	657	CD	LYS	A	460	4.982	22.089	10.797	1.00	31.10	A	C
ATOM	660	CE	LYS	A	460	5.641	21.091	11.756	1.00	33.59	A	C
ATOM	663	NZ	LYS	A	460	6.879	20.456	11.191	1.00	35.01	A	N
ATOM	667	C	LYS	A	460	1.301	24.390	11.917	1.00	25.65	A	C
ATOM	668	O	LYS	A	460	0.444	23.818	11.226	1.00	25.83	A	O
ATOM	669	N	LYS	A	461	1.574	25.687	11.808	1.00	25.80	A	N
ATOM	671	CA	LYS	A	461	0.826	26.538	10.882	1.00	26.62	A	C
ATOM	673	CB	LYS	A	461	1.252	28.006	11.008	1.00	26.88	A	C
ATOM	676	CG	LYS	A	461	2.713	28.253	10.821	1.00	27.10	A	C
ATOM	679	CD	LYS	A	461	2.998	29.749	10.885	1.00	26.75	A	C
ATOM	682	CE	LYS	A	461	4.299	30.069	10.215	1.00	26.14	A	C
ATOM	685	NZ	LYS	A	461	4.520	31.513	10.213	1.00	24.09	A	N
ATOM	689	C	LYS	A	461	0.920	26.065	9.424	1.00	26.93	A	C
ATOM	690	O	LYS	A	461	-0.036	26.221	8.675	1.00	27.53	A	O

ATOM	691	N	ASP	A	462	2.046	25.462	9.044	1.00	27.62	A	N
ATOM	693	CA	ASP	A	462	2.260	24.961	7.678	1.00	28.08	A	C
ATOM	695	CB	ASP	A	462	3.747	25.062	7.309	1.00	28.77	A	C
ATOM	698	CG	ASP	A	462	4.025	24.701	5.853	1.00	30.67	A	C
ATOM	699	OD1	ASP	A	462	3.273	25.156	4.964	1.00	33.53	A	O
ATOM	700	OD2	ASP	A	462	4.973	23.959	5.506	1.00	34.82	A	O
ATOM	701	C	ASP	A	462	1.772	23.509	7.560	1.00	27.68	A	C
ATOM	702	O	ASP	A	462	2.542	22.601	7.211	1.00	28.33	A	O
ATOM	703	N	CYS	A	463	0.500	23.302	7.891	1.00	26.54	A	N
ATOM	705	CA	CYS	A	463	-0.123	21.991	7.824	1.00	25.64	A	C
ATOM	707	CB	CYS	A	463	-0.529	21.522	9.217	1.00	25.87	A	C
ATOM	710	SG	CYS	A	463	-1.141	19.833	9.252	1.00	28.94	A	S
ATOM	711	C	CYS	A	463	-1.350	22.104	6.918	1.00	23.92	A	C
ATOM	712	O	CYS	A	463	-2.319	22.772	7.251	1.00	23.05	A	O
ATOM	713	N	THR	A	464	-1.277	21.480	5.751	1.00	22.41	A	N
ATOM	715	CA	THR	A	464	-2.385	21.500	4.800	1.00	21.51	A	C
ATOM	717	CB	THR	A	464	-1.947	20.928	3.435	1.00	21.47	A	C
ATOM	719	OG1	THR	A	464	-1.405	19.607	3.600	1.00	19.22	A	O
ATOM	721	CG2	THR	A	464	-0.804	21.743	2.823	1.00	21.55	A	C
ATOM	725	C	THR	A	464	-3.571	20.689	5.316	1.00	21.41	A	C
ATOM	726	O	THR	A	464	-3.414	19.755	6.111	1.00	19.82	A	O
ATOM	727	N	LEU	A	465	-4.758	21.040	4.832	1.00	21.68	A	N
ATOM	729	CA	LEU	A	465	-5.969	20.261	5.090	1.00	22.10	A	C
ATOM	731	CB	LEU	A	465	-7.165	20.906	4.378	1.00	22.26	A	C
ATOM	734	CG	LEU	A	465	-7.631	22.229	4.986	1.00	22.45	A	C
ATOM	736	CD1	LEU	A	465	-8.763	22.808	4.170	1.00	24.00	A	C
ATOM	740	CD2	LEU	A	465	-8.079	22.028	6.446	1.00	23.54	A	C
ATOM	744	C	LEU	A	465	-5.798	18.821	4.624	1.00	22.80	A	C
ATOM	745	O	LEU	A	465	-6.322	17.892	5.234	1.00	22.69	A	O
ATOM	746	N	ASP	A	466	-5.073	18.665	3.524	1.00	23.58	A	N
ATOM	748	CA	ASP	A	466	-4.666	17.367	3.004	1.00	25.03	A	C
ATOM	750	CB	ASP	A	466	-3.709	17.593	1.820	1.00	25.18	A	C
ATOM	753	CG	ASP	A	466	-3.414	16.332	1.038	1.00	27.16	A	C
ATOM	754	OD1	ASP	A	466	-3.623	15.216	1.570	1.00	26.35	A	O
ATOM	755	OD2	ASP	A	466	-2.966	16.376	-0.139	1.00	29.99	A	O
ATOM	756	C	ASP	A	466	-3.993	16.539	4.101	1.00	25.88	A	C
ATOM	757	O	ASP	A	466	-4.460	15.448	4.445	1.00	25.28	A	O
ATOM	758	N	ASN	A	467	-2.900	17.063	4.656	1.00	27.10	A	N
ATOM	760	CA	ASN	A	467	-2.161	16.350	5.702	1.00	28.05	A	C
ATOM	762	CB	ASN	A	467	-0.772	16.985	5.916	1.00	28.48	A	C
ATOM	765	CG	ASN	A	467	0.134	16.866	4.684	1.00	29.52	A	C
ATOM	766	OD1	ASN	A	467	0.992	17.713	4.447	1.00	31.12	A	O
ATOM	767	ND2	ASN	A	467	-0.059	15.816	3.901	1.00	33.05	A	N
ATOM	770	C	ASN	A	467	-2.920	16.263	7.037	1.00	28.75	A	C
ATOM	771	O	ASN	A	467	-2.724	15.322	7.806	1.00	28.72	A	O
ATOM	772	N	LYS	A	468	-3.794	17.232	7.296	1.00	29.65	A	N
ATOM	774	CA	LYS	A	468	-4.560	17.300	8.544	1.00	30.66	A	C
ATOM	776	CB	LYS	A	468	-5.273	18.642	8.639	1.00	30.86	A	C
ATOM	779	CG	LYS	A	468	-5.702	19.038	10.031	1.00	32.87	A	C
ATOM	782	CD	LYS	A	468	-4.950	20.278	10.513	1.00	35.25	A	C
ATOM	785	CE	LYS	A	468	-5.304	21.521	9.671	1.00	36.51	A	C
ATOM	788	NZ	LYS	A	468	-4.860	22.805	10.300	1.00	37.11	A	N
ATOM	792	C	LYS	A	468	-5.604	16.186	8.644	1.00	31.56	A	C
ATOM	793	O	LYS	A	468	-5.905	15.716	9.740	1.00	31.30	A	O
ATOM	794	N	GLU	A	469	-6.159	15.779	7.504	1.00	32.55	A	N
ATOM	796	CA	GLU	A	469	-7.144	14.694	7.473	1.00	33.52	A	C
ATOM	798	CB	GLU	A	469	-7.866	14.646	6.117	1.00	33.78	A	C
ATOM	801	CG	GLU	A	469	-8.835	13.476	5.924	1.00	34.57	A	C
ATOM	804	CD	GLU	A	469	-9.939	13.398	6.975	1.00	36.41	A	C
ATOM	805	OE1	GLU	A	469	-10.241	14.421	7.638	1.00	36.96	A	O
ATOM	806	OE2	GLU	A	469	-10.527	12.301	7.131	1.00	38.63	A	O
ATOM	807	C	GLU	A	469	-6.471	13.355	7.789	1.00	34.36	A	C
ATOM	808	O	GLU	A	469	-7.067	12.508	8.436	1.00	33.99	A	O
ATOM	809	N	LYS	A	470	-5.226	13.185	7.344	1.00	35.36	A	N
ATOM	811	CA	LYS	A	470	-4.441	11.983	7.651	1.00	36.27	A	C
ATOM	813	CB	LYS	A	470	-3.087	12.022	6.942	1.00	36.53	A	C
ATOM	816	CG	LYS	A	470	-3.155	12.204	5.444	1.00	37.48	A	C

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ATOM    819  CD  LYS A 470      -1.766  12.076   4.833  1.00 38.99      A    C
ATOM    822  CE  LYS A 470      -1.822  11.889   3.334  1.00 39.11      A    C
ATOM    825  NZ  LYS A 470      -0.566  11.286   2.828  1.00 39.24      A    N
ATOM    829  C   LYS A 470      -4.184  11.839   9.144  1.00 36.64      A    C
ATOM    830  O   LYS A 470      -4.342  10.758   9.709  1.00 37.23      A    O
ATOM    831  N   PHE A 471      -3.773  12.938   9.763  1.00 36.96      A    N
ATOM    833  CA  PHE A 471      -3.512  13.023  11.201  1.00 37.25      A    C
ATOM    835  CB  PHE A 471      -2.955  14.420  11.517  1.00 37.75      A    C
ATOM    838  CG  PHE A 471      -2.489  14.615  12.947  1.00 40.27      A    C
ATOM    839  CD1 PHE A 471      -1.834  13.605  13.650  1.00 42.26      A    C
ATOM    841  CE1 PHE A 471      -1.407  13.815  14.958  1.00 43.12      A    C
ATOM    843  CZ  PHE A 471      -1.611  15.056  15.572  1.00 43.43      A    C
ATOM    845  CE2 PHE A 471      -2.243  16.066  14.883  1.00 42.92      A    C
ATOM    847  CD2 PHE A 471      -2.680  15.847  13.578  1.00 42.50      A    C
ATOM    849  C   PHE A 471      -4.770  12.764  12.031  1.00 36.80      A    C
ATOM    850  O   PHE A 471      -4.725  12.035  13.017  1.00 36.85      A    O
ATOM    851  N   MET A 472      -5.885  13.369  11.630  1.00 36.07      A    N
ATOM    853  CA  MET A 472      -7.154  13.199  12.338  1.00 36.08      A    C
ATOM    855  CB  MET A 472      -8.246  14.103  11.761  1.00 36.21      A    C
ATOM    858  CG  MET A 472      -8.083  15.565  12.091  1.00 38.47      A    C
ATOM    861  SD  MET A 472      -7.642  15.859  13.819  1.00 42.21      A    S
ATOM    862  CE  MET A 472      -5.860  15.966  13.721  1.00 42.25      A    C
ATOM    866  C   MET A 472      -7.626  11.758  12.262  1.00 35.10      A    C
ATOM    867  O   MET A 472      -8.011  11.176  13.278  1.00 34.68      A    O
ATOM    868  N   SER A 473      -7.599  11.200  11.056  1.00 34.38      A    N
ATOM    870  CA  SER A 473      -8.067   9.836  10.838  1.00 34.10      A    C
ATOM    872  CB  SER A 473      -8.111   9.481   9.341  1.00 34.17      A    C
ATOM    875  OG  SER A 473      -6.876   9.725   8.700  1.00 35.90      A    O
ATOM    877  C   SER A 473      -7.194   8.870  11.619  1.00 33.23      A    C
ATOM    878  O   SER A 473      -7.681   7.877  12.146  1.00 33.23      A    O
ATOM    879  N   GLU A 474      -5.909   9.196  11.728  1.00 32.29      A    N
ATOM    881  CA  GLU A 474      -4.957   8.405  12.504  1.00 31.53      A    C
ATOM    883  CB  GLU A 474      -3.532   8.889  12.235  1.00 32.06      A    C
ATOM    886  CG  GLU A 474      -2.462   8.083  12.940  1.00 35.27      A    C
ATOM    889  CD  GLU A 474      -1.059   8.482  12.520  1.00 38.82      A    C
ATOM    890  OE1 GLU A 474      -0.125   7.684  12.765  1.00 41.03      A    O
ATOM    891  OE2 GLU A 474      -0.896   9.590  11.945  1.00 41.72      A    O
ATOM    892  C   GLU A 474      -5.252   8.474  13.999  1.00 29.52      A    C
ATOM    893  O   GLU A 474      -5.194   7.463  14.689  1.00 28.59      A    O
ATOM    894  N   ALA A 475      -5.583   9.664  14.486  1.00 27.61      A    N
ATOM    896  CA  ALA A 475      -5.852   9.876  15.908  1.00 26.39      A    C
ATOM    898  CB  ALA A 475      -5.991  11.361  16.196  1.00 26.28      A    C
ATOM    902  C   ALA A 475      -7.117   9.144  16.379  1.00 25.41      A    C
ATOM    903  O   ALA A 475      -7.186   8.717  17.521  1.00 24.68      A    O
ATOM    904  N   VAL A 476      -8.111   9.024  15.501  1.00 24.57      A    N
ATOM    906  CA  VAL A 476      -9.364   8.342  15.837  1.00 24.02      A    C
ATOM    908  CB  VAL A 476     -10.457   8.593  14.764  1.00 24.14      A    C
ATOM    910  CG1 VAL A 476     -11.668   7.695  14.975  1.00 24.34      A    C
ATOM    914  CG2 VAL A 476     -10.910  10.051  14.786  1.00 24.76      A    C
ATOM    918  C   VAL A 476      -9.096   6.840  16.010  1.00 23.50      A    C
ATOM    919  O   VAL A 476      -9.673   6.207  16.889  1.00 22.85      A    O
ATOM    920  N   ILE A 477      -8.191   6.283  15.197  1.00 23.32      A    N
ATOM    922  CA  ILE A 477      -7.794   4.880  15.366  1.00 23.29      A    C
ATOM    924  CB  ILE A 477      -6.857   4.392  14.232  1.00 23.54      A    C
ATOM    926  CG1 ILE A 477      -7.579   4.420  12.883  1.00 25.55      A    C
ATOM    929  CD1 ILE A 477      -6.693   4.070  11.676  1.00 26.07      A    C
ATOM    933  CG2 ILE A 477      -6.357   2.978  14.550  1.00 24.90      A    C
ATOM    937  C   ILE A 477      -7.126   4.693  16.729  1.00 22.19      A    C
ATOM    938  O   ILE A 477      -7.505   3.833  17.502  1.00 20.75      A    O
ATOM    939  N   MET A 478      -6.126   5.518  17.025  1.00 22.05      A    N
ATOM    941  CA  MET A 478      -5.479   5.507  18.341  1.00 21.67      A    C
ATOM    943  CB  MET A 478      -4.401   6.603  18.421  1.00 22.21      A    C
ATOM    946  CG  MET A 478      -3.172   6.370  17.537  1.00 23.35      A    C
ATOM    949  SD  MET A 478      -2.324   4.761  17.784  1.00 27.04      A    S
ATOM    950  CE  MET A 478      -1.687   4.917  19.390  1.00 24.74      A    C
ATOM    954  C   MET A 478      -6.463   5.660  19.508  1.00 21.22      A    C
ATOM    955  O   MET A 478      -6.280   5.042  20.541  1.00 20.80      A    O
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ATOM    956  N   LYS A 479      -7.517   6.461  19.336  1.00 21.22      A    N
ATOM    958  CA  LYS A 479      -8.521   6.681  20.381  1.00 21.07      A    C
ATOM    960  CB  LYS A 479      -9.550   7.727  19.910  1.00 21.83      A    C
ATOM    963  CG  LYS A 479     -10.728   7.940  20.864  1.00 25.29      A    C
ATOM    966  CD  LYS A 479     -11.616   9.074  20.401  1.00 28.79      A    C
ATOM    969  CE  LYS A 479     -12.585   9.512  21.494  1.00 30.50      A    C
ATOM    972  NZ  LYS A 479     -13.545   8.454  21.868  1.00 31.90      A    N
ATOM    976  C   LYS A 479      -9.251   5.394  20.752  1.00 20.32      A    C
ATOM    977  O   LYS A 479      -9.653   5.195  21.906  1.00 20.37      A    O
ATOM    978  N   ASN A 480      -9.447   4.529  19.761  1.00 18.51      A    N
ATOM    980  CA  ASN A 480     -10.168   3.284  19.980  1.00 18.01      A    C
ATOM    982  CB  ASN A 480     -10.851   2.841  18.692  1.00 17.94      A    C
ATOM    985  CG  ASN A 480     -12.098   3.625  18.410  1.00 16.43      A    C
ATOM    986  OD1 ASN A 480     -13.135   3.388  19.038  1.00 14.27      A    O
ATOM    987  ND2 ASN A 480     -12.016   4.574  17.481  1.00 13.64      A    N
ATOM    990  C   ASN A 480      -9.277   2.174  20.512  1.00 17.93      A    C
ATOM    991  O   ASN A 480      -9.768   1.196  21.049  1.00 17.90      A    O
ATOM    992  N   LEU A 481      -7.969   2.305  20.345  1.00 18.54      A    N
ATOM    994  CA  LEU A 481      -7.052   1.344  20.933  1.00 19.58      A    C
ATOM    996  CB  LEU A 481      -5.647   1.510  20.375  1.00 19.65      A    C
ATOM    999  CG  LEU A 481      -5.418   0.995  18.958  1.00 19.49      A    C
ATOM   1001  CD1 LEU A 481      -4.028   1.362  18.492  1.00 20.75      A    C
ATOM   1005  CD2 LEU A 481      -5.645  -0.497  18.891  1.00 19.12      A    C
ATOM   1009  C   LEU A 481      -7.028   1.560  22.430  1.00 20.27      A    C
ATOM   1010  O   LEU A 481      -6.658   2.630  22.899  1.00 22.42      A    O
ATOM   1011  N   ASP A 482      -7.411   0.543  23.177  1.00 20.28      A    N
ATOM   1013  CA  ASP A 482      -7.360   0.583  24.626  1.00 20.20      A    C
ATOM   1015  CB  ASP A 482      -8.781   0.626  25.196  1.00 21.36      A    C
ATOM   1018  CG  ASP A 482      -8.815   0.831  26.702  1.00 24.17      A    C
ATOM   1019  OD1 ASP A 482      -9.901   0.603  27.288  1.00 31.84      A    O
ATOM   1020  OD2 ASP A 482      -7.843   1.228  27.382  1.00 28.34      A    O
ATOM   1021  C   ASP A 482      -6.625  -0.664  25.080  1.00 19.09      A    C
ATOM   1022  O   ASP A 482      -7.178  -1.765  25.073  1.00 19.88      A    O
ATOM   1023  N   HIS A 483      -5.349  -0.490  25.413  1.00 16.36      A    N
ATOM   1025  CA  HIS A 483      -4.508  -1.572  25.890  1.00 15.18      A    C
ATOM   1027  CB  HIS A 483      -3.723  -2.178  24.727  1.00 14.01      A    C
ATOM   1030  CG  HIS A 483      -3.068  -3.474  25.069  1.00 13.88      A    C
ATOM   1031  ND1 HIS A 483      -1.872  -3.542  25.755  1.00 13.01      A    N
ATOM   1033  CE1 HIS A 483      -1.569  -4.812  25.969  1.00 13.34      A    C
ATOM   1035  NE2 HIS A 483      -2.515  -5.566  25.429  1.00 12.59      A    N
ATOM   1037  CD2 HIS A 483      -3.465  -4.752  24.867  1.00 12.02      A    C
ATOM   1039  C   HIS A 483      -3.553  -1.015  26.964  1.00 14.57      A    C
ATOM   1040  O   HIS A 483      -3.092   0.118  26.840  1.00 14.09      A    O
ATOM   1041  N   PRO A 484      -3.278  -1.775  28.023  1.00 14.32      A    N
ATOM   1042  CA  PRO A 484      -2.360  -1.310  29.080  1.00 13.52      A    C
ATOM   1044  CB  PRO A 484      -2.254  -2.519  30.037  1.00 14.18      A    C
ATOM   1047  CG  PRO A 484      -3.355  -3.429  29.700  1.00 15.62      A    C
ATOM   1050  CD  PRO A 484      -3.866  -3.091  28.339  1.00 14.94      A    C
ATOM   1053  C   PRO A 484      -0.956  -0.924  28.610  1.00 12.37      A    C
ATOM   1054  O   PRO A 484      -0.285  -0.173  29.308  1.00 12.09      A    O
ATOM   1055  N   HIS A 485      -0.532  -1.423  27.448  1.00 11.71      A    N
ATOM   1057  CA  HIS A 485       0.790  -1.148  26.915  1.00 10.90      A    C
ATOM   1059  CB  HIS A 485       1.606  -2.438  26.948  1.00 11.48      A    C
ATOM   1062  CG  HIS A 485       1.687  -2.999  28.326  1.00 11.67      A    C
ATOM   1063  ND1 HIS A 485       2.263  -2.293  29.357  1.00 10.00      A    N
ATOM   1065  CE1 HIS A 485       2.139  -2.984  30.478  1.00 13.83      A    C
ATOM   1067  NE2 HIS A 485       1.496  -4.105  30.211  1.00 13.41      A    N
ATOM   1069  CD2 HIS A 485       1.179  -4.129  28.873  1.00 13.59      A    C
ATOM   1071  C   HIS A 485       0.786  -0.514  25.549  1.00 10.49      A    C
ATOM   1072  O   HIS A 485       1.722  -0.706  24.795  1.00  9.78      A    O
ATOM   1073  N   ILE A 486      -0.267   0.258  25.260  1.00  9.75      A    N
ATOM   1075  CA  ILE A 486      -0.313   1.165  24.107  1.00  9.72      A    C
ATOM   1077  CB  ILE A 486      -1.352   0.675  23.077  1.00  9.49      A    C
ATOM   1079  CG1 ILE A 486      -0.941  -0.698  22.509  1.00  9.88      A    C
ATOM   1082  CD1 ILE A 486      -1.944  -1.282  21.569  1.00 11.12      A    C
ATOM   1086  CG2 ILE A 486      -1.516   1.670  21.927  1.00 10.54      A    C
ATOM   1090  C   ILE A 486      -0.683   2.561  24.617  1.00 10.03      A    C
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ATOM	1091	O	ILE	A	486	-1.500	2.684	25.533	1.00	9.12	A	O
ATOM	1092	N	VAL	A	487	-0.079	3.585	24.034	1.00	10.75	A	N
ATOM	1094	CA	VAL	A	487	-0.294	4.958	24.477	1.00	11.70	A	C
ATOM	1096	CB	VAL	A	487	0.535	6.007	23.674	1.00	11.46	A	C
ATOM	1098	CG1	VAL	A	487	2.006	5.849	23.946	1.00	11.31	A	C
ATOM	1102	CG2	VAL	A	487	0.242	5.925	22.175	1.00	12.24	A	C
ATOM	1106	C	VAL	A	487	-1.782	5.278	24.394	1.00	12.42	A	C
ATOM	1107	O	VAL	A	487	-2.479	4.824	23.481	1.00	10.87	A	O
ATOM	1108	N	LYS	A	488	-2.269	6.010	25.386	1.00	14.04	A	N
ATOM	1110	CA	LYS	A	488	-3.699	6.252	25.531	1.00	15.40	A	C
ATOM	1112	CB	LYS	A	488	-4.147	6.081	26.979	1.00	16.29	A	C
ATOM	1115	CG	LYS	A	488	-5.648	6.355	27.161	1.00	18.92	A	C
ATOM	1118	CD	LYS	A	488	-6.109	6.153	28.588	1.00	22.97	A	C
ATOM	1121	CE	LYS	A	488	-7.638	6.269	28.693	1.00	26.06	A	C
ATOM	1124	NZ	LYS	A	488	-8.179	5.734	29.994	1.00	28.52	A	N
ATOM	1128	C	LYS	A	488	-4.019	7.663	25.090	1.00	16.61	A	C
ATOM	1129	O	LYS	A	488	-3.470	8.625	25.650	1.00	15.54	A	O
ATOM	1130	N	LEU	A	489	-4.879	7.760	24.079	1.00	18.15	A	N
ATOM	1132	CA	LEU	A	489	-5.458	9.028	23.644	1.00	20.47	A	C
ATOM	1134	CB	LEU	A	489	-5.707	9.035	22.135	1.00	20.96	A	C
ATOM	1137	CG	LEU	A	489	-6.318	10.312	21.519	1.00	22.08	A	C
ATOM	1139	CD1	LEU	A	489	-6.157	10.316	20.034	1.00	23.52	A	C
ATOM	1143	CD2	LEU	A	489	-7.776	10.472	21.876	1.00	24.93	A	C
ATOM	1147	C	LEU	A	489	-6.734	9.229	24.426	1.00	22.11	A	C
ATOM	1148	O	LEU	A	489	-7.625	8.370	24.402	1.00	23.38	A	O
ATOM	1149	N	ILE	A	490	-6.813	10.361	25.125	1.00	22.70	A	N
ATOM	1151	CA	ILE	A	490	-7.920	10.685	26.016	1.00	23.88	A	C
ATOM	1153	CB	ILE	A	490	-7.400	11.539	27.185	1.00	24.15	A	C
ATOM	1155	CG1	ILE	A	490	-6.437	10.714	28.049	1.00	25.63	A	C
ATOM	1158	CD1	ILE	A	490	-5.849	11.484	29.192	1.00	25.52	A	C
ATOM	1162	CG2	ILE	A	490	-8.558	12.096	28.022	1.00	25.12	A	C
ATOM	1166	C	ILE	A	490	-9.047	11.420	25.274	1.00	23.99	A	C
ATOM	1167	O	ILE	A	490	-10.232	11.098	25.448	1.00	24.52	A	O
ATOM	1168	N	GLY	A	491	-8.685	12.413	24.468	1.00	23.22	A	N
ATOM	1170	CA	GLY	A	491	-9.677	13.139	23.681	1.00	23.44	A	C
ATOM	1173	C	GLY	A	491	-9.145	13.889	22.481	1.00	23.06	A	C
ATOM	1174	O	GLY	A	491	-7.944	14.066	22.320	1.00	21.24	A	O
ATOM	1175	N	ILE	A	492	-10.069	14.324	21.623	1.00	23.34	A	N
ATOM	1177	CA	ILE	A	492	-9.747	15.175	20.490	1.00	23.94	A	C
ATOM	1179	CB	ILE	A	492	-9.914	14.394	19.167	1.00	24.29	A	C
ATOM	1181	CG1	ILE	A	492	-9.044	13.128	19.175	1.00	24.89	A	C
ATOM	1184	CD1	ILE	A	492	-9.389	12.139	18.099	1.00	26.68	A	C
ATOM	1188	CG2	ILE	A	492	-9.539	15.252	17.986	1.00	24.59	A	C
ATOM	1192	C	ILE	A	492	-10.675	16.401	20.528	1.00	24.76	A	C
ATOM	1193	O	ILE	A	492	-11.891	16.254	20.639	1.00	23.89	A	O
ATOM	1194	N	ILE	A	493	-10.086	17.598	20.508	1.00	25.52	A	N
ATOM	1196	CA	ILE	A	493	-10.828	18.833	20.257	1.00	26.54	A	C
ATOM	1198	CB	ILE	A	493	-10.315	20.009	21.138	1.00	26.60	A	C
ATOM	1200	CG1	ILE	A	493	-10.215	19.614	22.613	1.00	26.82	A	C
ATOM	1203	CD1	ILE	A	493	-11.446	18.990	23.180	1.00	27.58	A	C
ATOM	1207	CG2	ILE	A	493	-11.217	21.249	20.961	1.00	26.95	A	C
ATOM	1211	C	ILE	A	493	-10.609	19.151	18.785	1.00	27.17	A	C
ATOM	1212	O	ILE	A	493	-9.531	19.576	18.404	1.00	26.34	A	O
ATOM	1213	N	GLU	A	494	-11.628	18.927	17.959	1.00	28.32	A	N
ATOM	1215	CA	GLU	A	494	-11.502	19.096	16.510	1.00	29.45	A	C
ATOM	1217	CB	GLU	A	494	-12.698	18.444	15.800	1.00	30.09	A	C
ATOM	1220	CG	GLU	A	494	-12.800	16.943	16.024	1.00	32.11	A	C
ATOM	1223	CD	GLU	A	494	-13.958	16.292	15.280	1.00	35.78	A	C
ATOM	1224	OE1	GLU	A	494	-14.108	16.531	14.058	1.00	38.41	A	O
ATOM	1225	OE2	GLU	A	494	-14.717	15.524	15.918	1.00	38.33	A	O
ATOM	1226	C	GLU	A	494	-11.390	20.567	16.098	1.00	29.72	A	C
ATOM	1227	O	GLU	A	494	-10.667	20.900	15.160	1.00	29.12	A	O
ATOM	1228	N	GLU	A	495	-12.073	21.432	16.846	1.00	30.47	A	N
ATOM	1230	CA	GLU	A	495	-12.259	22.853	16.505	1.00	31.12	A	C
ATOM	1232	CB	GLU	A	495	-13.324	23.465	17.435	1.00	31.66	A	C
ATOM	1235	CG	GLU	A	495	-14.759	23.024	17.203	1.00	34.10	A	C
ATOM	1238	CD	GLU	A	495	-14.995	21.541	17.444	1.00	36.85	A	C

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ATOM   1239  OE1 GLU A 495     -14.650  21.029  18.544  1.00 38.24      A    O
ATOM   1240  OE2 GLU A 495     -15.521  20.885  16.517  1.00 39.02      A    O
ATOM   1241  C   GLU A 495     -10.978  23.695  16.633  1.00 30.92      A    C
ATOM   1242  O   GLU A 495      -9.950  23.203  17.113  1.00 30.08      A    O
ATOM   1243  N   GLU A 496     -11.084  24.966  16.207  1.00 30.74      A    N
ATOM   1245  CA  GLU A 496     -10.102  26.053  16.450  1.00 30.21      A    C
ATOM   1247  CB  GLU A 496     -10.331  26.722  17.809  1.00 30.71      A    C
ATOM   1250  CG  GLU A 496     -11.767  27.153  18.080  1.00 33.56      A    C
ATOM   1253  CD  GLU A 496     -12.218  28.297  17.176  1.00 37.40      A    C
ATOM   1254  OE1 GLU A 496     -11.734  29.442  17.368  1.00 39.71      A    O
ATOM   1255  OE2 GLU A 496     -13.057  28.053  16.273  1.00 39.53      A    O
ATOM   1256  C   GLU A 496      -8.688  25.536  16.214  1.00 28.69      A    C
ATOM   1257  O   GLU A 496      -8.518  24.890  15.181  1.00 29.82      A    O
ATOM   1258  N   PRO A 497      -7.673  25.765  17.068  1.00 26.40      A    N
ATOM   1259  CA  PRO A 497      -6.463  24.955  16.914  1.00 24.97      A    C
ATOM   1261  CB  PRO A 497      -5.435  25.650  17.812  1.00 25.01      A    C
ATOM   1264  CG  PRO A 497      -6.217  26.352  18.819  1.00 25.48      A    C
ATOM   1267  CD  PRO A 497      -7.508  26.726  18.176  1.00 26.20      A    C
ATOM   1270  C   PRO A 497      -6.785  23.545  17.400  1.00 23.59      A    C
ATOM   1271  O   PRO A 497      -7.238  23.365  18.525  1.00 21.60      A    O
ATOM   1272  N   THR A 498      -6.593  22.562  16.533  1.00 22.37      A    N
ATOM   1274  CA  THR A 498      -6.969  21.193  16.855  1.00 22.15      A    C
ATOM   1276  CB  THR A 498      -6.918  20.363  15.580  1.00 22.32      A    C
ATOM   1278  OG1 THR A 498      -7.958  20.826  14.700  1.00 25.57      A    O
ATOM   1280  CG2 THR A 498      -7.252  18.924  15.840  1.00 22.92      A    C
ATOM   1284  C   THR A 498      -6.022  20.654  17.922  1.00 20.09      A    C
ATOM   1285  O   THR A 498      -4.835  20.874  17.821  1.00 19.92      A    O
ATOM   1286  N   TRP A 499      -6.568  20.002  18.950  1.00 19.00      A    N
ATOM   1288  CA  TRP A 499      -5.777  19.413  20.040  1.00 17.23      A    C
ATOM   1290  CB  TRP A 499      -6.188  20.010  21.393  1.00 17.26      A    C
ATOM   1293  CG  TRP A 499      -5.734  21.440  21.693  1.00 16.11      A    C
ATOM   1294  CD1 TRP A 499      -5.098  22.301  20.851  1.00 16.58      A    C
ATOM   1296  NE1 TRP A 499      -4.865  23.499  21.483  1.00 15.91      A    N
ATOM   1298  CE2 TRP A 499      -5.342  23.431  22.760  1.00 13.91      A    C
ATOM   1299  CD2 TRP A 499      -5.906  22.149  22.927  1.00 14.32      A    C
ATOM   1300  CE3 TRP A 499      -6.474  21.825  24.167  1.00 14.41      A    C
ATOM   1302  CZ3 TRP A 499      -6.466  22.789  25.187  1.00 15.48      A    C
ATOM   1304  CH2 TRP A 499      -5.914  24.063  24.973  1.00 15.79      A    C
ATOM   1306  CZ2 TRP A 499      -5.345  24.401  23.770  1.00 16.05      A    C
ATOM   1308  C   TRP A 499      -6.011  17.891  20.113  1.00 16.56      A    C
ATOM   1309  O   TRP A 499      -7.161  17.444  20.219  1.00 16.56      A    O
ATOM   1310  N   ILE A 500      -4.933  17.111  20.082  1.00 15.45      A    N
ATOM   1312  CA  ILE A 500      -4.987  15.696  20.427  1.00 15.58      A    C
ATOM   1314  CB  ILE A 500      -4.126  14.870  19.461  1.00 16.46      A    C
ATOM   1316  CG1 ILE A 500      -4.423  15.233  17.994  1.00 17.06      A    C
ATOM   1319  CD1 ILE A 500      -5.887  15.183  17.626  1.00 18.75      A    C
ATOM   1323  CG2 ILE A 500      -4.288  13.390  19.744  1.00 18.35      A    C
ATOM   1327  C   ILE A 500      -4.467  15.555  21.863  1.00 14.87      A    C
ATOM   1328  O   ILE A 500      -3.323  15.879  22.141  1.00 14.70      A    O
ATOM   1329  N   ILE A 501      -5.318  15.096  22.765  1.00 13.73      A    N
ATOM   1331  CA  ILE A 501      -4.998  14.985  24.178  1.00 13.36      A    C
ATOM   1333  CB  ILE A 501      -6.190  15.451  25.034  1.00 12.71      A    C
ATOM   1335  CG1 ILE A 501      -6.719  16.788  24.496  1.00 14.26      A    C
ATOM   1338  CD1 ILE A 501      -7.978  17.256  25.129  1.00 15.07      A    C
ATOM   1342  CG2 ILE A 501      -5.768  15.583  26.483  1.00 12.38      A    C
ATOM   1346  C   ILE A 501      -4.629  13.546  24.539  1.00 13.36      A    C
ATOM   1347  O   ILE A 501      -5.469  12.638  24.448  1.00 13.51      A    O
ATOM   1348  N   MET A 502      -3.372  13.359  24.933  1.00 13.48      A    N
ATOM   1350  CA  MET A 502      -2.836  12.061  25.353  1.00 13.96      A    C
ATOM   1352  CB  MET A 502      -1.550  11.754  24.585  1.00 14.71      A    C
ATOM   1355  CG  MET A 502      -1.634  11.957  23.074  1.00 18.44      A    C
ATOM   1358  SD  MET A 502      -2.691  10.736  22.262  1.00 25.96      A    S
ATOM   1359  CE  MET A 502      -1.705   9.251  22.464  1.00 24.95      A    C
ATOM   1363  C   MET A 502      -2.498  12.057  26.845  1.00 13.14      A    C
ATOM   1364  O   MET A 502      -2.200  13.092  27.436  1.00 11.75      A    O
ATOM   1365  N   GLU A 503      -2.501  10.879  27.458  1.00 12.97      A    N
ATOM   1367  CA  GLU A 503      -1.947  10.721  28.784  1.00 13.82      A    C
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ATOM	1369	CB	GLU	A	503	-2.136	9.258	29.215	1.00	15.08	A	C
ATOM	1372	CG	GLU	A	503	-1.603	8.887	30.583	1.00	18.56	A	C
ATOM	1375	CD	GLU	A	503	-2.097	7.516	31.024	1.00	23.89	A	C
ATOM	1376	OE1	GLU	A	503	-2.315	6.636	30.153	1.00	26.84	A	O
ATOM	1377	OE2	GLU	A	503	-2.272	7.314	32.243	1.00	29.32	A	O
ATOM	1378	C	GLU	A	503	-0.457	11.112	28.747	1.00	13.19	A	C
ATOM	1379	O	GLU	A	503	0.230	10.778	27.787	1.00	13.15	A	O
ATOM	1380	N	LEU	A	504	0.020	11.836	29.760	1.00	12.59	A	N
ATOM	1382	CA	LEU	A	504	1.440	12.210	29.862	1.00	13.43	A	C
ATOM	1384	CB	LEU	A	504	1.635	13.449	30.746	1.00	13.57	A	C
ATOM	1387	CG	LEU	A	504	3.065	13.981	30.844	1.00	14.83	A	C
ATOM	1389	CD1	LEU	A	504	3.440	14.719	29.551	1.00	15.70	A	C
ATOM	1393	CD2	LEU	A	504	3.281	14.893	32.069	1.00	17.43	A	C
ATOM	1397	C	LEU	A	504	2.237	11.049	30.443	1.00	13.16	A	C
ATOM	1398	O	LEU	A	504	1.831	10.448	31.436	1.00	12.13	A	O
ATOM	1399	N	TYR	A	505	3.361	10.740	29.807	1.00	13.87	A	N
ATOM	1401	CA	TYR	A	505	4.261	9.682	30.247	1.00	14.37	A	C
ATOM	1403	CB	TYR	A	505	4.379	8.582	29.159	1.00	15.13	A	C
ATOM	1406	CG	TYR	A	505	3.034	7.948	28.815	1.00	14.57	A	C
ATOM	1407	CD1	TYR	A	505	2.254	7.352	29.802	1.00	16.24	A	C
ATOM	1409	CE1	TYR	A	505	0.996	6.804	29.506	1.00	15.83	A	C
ATOM	1411	CZ	TYR	A	505	0.517	6.853	28.221	1.00	13.11	A	C
ATOM	1412	OH	TYR	A	505	-0.713	6.332	27.933	1.00	15.41	A	O
ATOM	1414	CE2	TYR	A	505	1.255	7.455	27.229	1.00	13.32	A	C
ATOM	1416	CD2	TYR	A	505	2.506	8.017	27.532	1.00	14.19	A	C
ATOM	1418	C	TYR	A	505	5.566	10.408	30.557	1.00	14.61	A	C
ATOM	1419	O	TYR	A	505	6.379	10.672	29.675	1.00	13.90	A	O
ATOM	1420	N	PRO	A	506	5.707	10.836	31.812	1.00	15.51	A	N
ATOM	1421	CA	PRO	A	506	6.699	11.840	32.188	1.00	15.79	A	C
ATOM	1423	CB	PRO	A	506	6.291	12.186	33.616	1.00	16.40	A	C
ATOM	1426	CG	PRO	A	506	5.692	10.962	34.115	1.00	16.38	A	C
ATOM	1429	CD	PRO	A	506	4.903	10.414	32.974	1.00	16.03	A	C
ATOM	1432	C	PRO	A	506	8.168	11.364	32.119	1.00	15.41	A	C
ATOM	1433	O	PRO	A	506	9.055	12.186	32.029	1.00	15.80	A	O
ATOM	1434	N	TYR	A	507	8.406	10.062	32.106	1.00	14.60	A	N
ATOM	1436	CA	TYR	A	507	9.767	9.548	31.946	1.00	13.73	A	C
ATOM	1438	CB	TYR	A	507	9.872	8.143	32.516	1.00	13.74	A	C
ATOM	1441	CG	TYR	A	507	9.659	8.071	33.997	1.00	14.65	A	C
ATOM	1442	CD1	TYR	A	507	10.704	8.269	34.879	1.00	15.68	A	C
ATOM	1444	CE1	TYR	A	507	10.505	8.191	36.268	1.00	17.32	A	C
ATOM	1446	CZ	TYR	A	507	9.241	7.931	36.754	1.00	16.75	A	C
ATOM	1447	OH	TYR	A	507	9.002	7.873	38.099	1.00	19.60	A	O
ATOM	1449	CE2	TYR	A	507	8.198	7.737	35.895	1.00	15.81	A	C
ATOM	1451	CD2	TYR	A	507	8.408	7.807	34.521	1.00	14.55	A	C
ATOM	1453	C	TYR	A	507	10.276	9.550	30.491	1.00	13.31	A	C
ATOM	1454	O	TYR	A	507	11.451	9.268	30.268	1.00	13.27	A	O
ATOM	1455	N	GLY	A	508	9.411	9.838	29.516	1.00	12.24	A	N
ATOM	1457	CA	GLY	A	508	9.834	10.058	28.142	1.00	12.21	A	C
ATOM	1460	C	GLY	A	508	10.112	8.784	27.362	1.00	11.49	A	C
ATOM	1461	O	GLY	A	508	9.628	7.729	27.727	1.00	10.44	A	O
ATOM	1462	N	GLU	A	509	10.885	8.896	26.281	1.00	11.21	A	N
ATOM	1464	CA	GLU	A	509	11.183	7.744	25.416	1.00	11.54	A	C
ATOM	1466	CB	GLU	A	509	11.913	8.194	24.156	1.00	12.66	A	C
ATOM	1469	CG	GLU	A	509	11.143	9.164	23.279	1.00	15.29	A	C
ATOM	1472	CD	GLU	A	509	11.973	9.695	22.119	1.00	18.15	A	C
ATOM	1473	OE1	GLU	A	509	13.122	9.251	21.947	1.00	19.31	A	O
ATOM	1474	OE2	GLU	A	509	11.472	10.588	21.393	1.00	21.32	A	O
ATOM	1475	C	GLU	A	509	12.038	6.666	26.095	1.00	10.37	A	C
ATOM	1476	O	GLU	A	509	12.953	6.974	26.847	1.00	10.56	A	O
ATOM	1477	N	LEU	A	510	11.742	5.399	25.791	1.00	9.52	A	N
ATOM	1479	CA	LEU	A	510	12.447	4.275	26.392	1.00	9.25	A	C
ATOM	1481	CB	LEU	A	510	11.768	2.956	25.990	1.00	9.16	A	C
ATOM	1484	CG	LEU	A	510	12.395	1.682	26.566	1.00	8.82	A	C
ATOM	1486	CD1	LEU	A	510	12.453	1.737	28.081	1.00	9.86	A	C
ATOM	1490	CD2	LEU	A	510	11.596	0.465	26.104	1.00	9.45	A	C
ATOM	1494	C	LEU	A	510	13.948	4.249	26.057	1.00	9.51	A	C
ATOM	1495	O	LEU	A	510	14.772	3.937	26.925	1.00	9.34	A	O

ATOM	1496	N	GLY	A	511	14.322	4.610	24.824	1.00	9.82	A	N
ATOM	1498	CA	GLY	A	511	15.729	4.549	24.433	1.00	10.57	A	C
ATOM	1501	C	GLY	A	511	16.585	5.425	25.340	1.00	10.99	A	C
ATOM	1502	O	GLY	A	511	17.566	4.964	25.934	1.00	11.11	A	O
ATOM	1503	N	HIS	A	512	16.178	6.672	25.492	1.00	11.55	A	N
ATOM	1505	CA	HIS	A	512	16.875	7.608	26.374	1.00	12.69	A	C
ATOM	1507	CB	HIS	A	512	16.319	9.011	26.174	1.00	13.88	A	C
ATOM	1510	CG	HIS	A	512	16.559	9.541	24.795	1.00	17.28	A	C
ATOM	1511	ND1	HIS	A	512	17.678	9.214	24.061	1.00	22.03	A	N
ATOM	1513	CE1	HIS	A	512	17.618	9.808	22.882	1.00	22.98	A	C
ATOM	1515	NE2	HIS	A	512	16.508	10.518	22.831	1.00	21.48	A	N
ATOM	1517	CD2	HIS	A	512	15.821	10.360	24.011	1.00	20.94	A	C
ATOM	1519	C	HIS	A	512	16.810	7.196	27.840	1.00	11.73	A	C
ATOM	1520	O	HIS	A	512	17.795	7.308	28.560	1.00	11.30	A	O
ATOM	1521	N	TYR	A	513	15.664	6.682	28.269	1.00	10.95	A	N
ATOM	1523	CA	TYR	A	513	15.472	6.184	29.630	1.00	10.24	A	C
ATOM	1525	CB	TYR	A	513	14.034	5.677	29.797	1.00	10.11	A	C
ATOM	1528	CG	TYR	A	513	13.693	5.094	31.169	1.00	9.46	A	C
ATOM	1529	CD1	TYR	A	513	13.157	5.901	32.160	1.00	9.43	A	C
ATOM	1531	CE1	TYR	A	513	12.800	5.391	33.393	1.00	9.59	A	C
ATOM	1533	CZ	TYR	A	513	12.988	4.068	33.671	1.00	9.14	A	C
ATOM	1534	OH	TYR	A	513	12.628	3.617	34.912	1.00	12.42	A	O
ATOM	1536	CE2	TYR	A	513	13.533	3.214	32.708	1.00	8.34	A	C
ATOM	1538	CD2	TYR	A	513	13.854	3.735	31.452	1.00	8.09	A	C
ATOM	1540	C	TYR	A	513	16.469	5.068	29.965	1.00	10.47	A	C
ATOM	1541	O	TYR	A	513	17.110	5.099	31.009	1.00	10.13	A	O
ATOM	1542	N	LEU	A	514	16.623	4.102	29.058	1.00	10.69	A	N
ATOM	1544	CA	LEU	A	514	17.596	3.021	29.239	1.00	11.38	A	C
ATOM	1546	CB	LEU	A	514	17.478	1.997	28.115	1.00	11.46	A	C
ATOM	1549	CG	LEU	A	514	16.163	1.198	28.035	1.00	12.98	A	C
ATOM	1551	CD1	LEU	A	514	16.082	0.442	26.729	1.00	14.53	A	C
ATOM	1555	CD2	LEU	A	514	16.010	0.260	29.218	1.00	12.92	A	C
ATOM	1559	C	LEU	A	514	19.027	3.556	29.300	1.00	12.00	A	C
ATOM	1560	O	LEU	A	514	19.839	3.080	30.090	1.00	12.23	A	O
ATOM	1561	N	GLU	A	515	19.330	4.518	28.450	1.00	12.66	A	N
ATOM	1563	CA	GLU	A	515	20.650	5.160	28.447	1.00	14.53	A	C
ATOM	1565	CB	GLU	A	515	20.742	6.212	27.346	1.00	15.14	A	C
ATOM	1568	CG	GLU	A	515	20.701	5.656	25.929	1.00	19.10	A	C
ATOM	1571	CD	GLU	A	515	20.531	6.744	24.868	1.00	24.40	A	C
ATOM	1572	OE1	GLU	A	515	20.496	7.948	25.236	1.00	29.66	A	O
ATOM	1573	OE2	GLU	A	515	20.433	6.395	23.665	1.00	28.24	A	O
ATOM	1574	C	GLU	A	515	20.954	5.812	29.795	1.00	15.17	A	C
ATOM	1575	O	GLU	A	515	22.046	5.601	30.347	1.00	15.52	A	O
ATOM	1576	N	ARG	A	516	19.987	6.576	30.317	1.00	15.35	A	N
ATOM	1578	CA	ARG	A	516	20.114	7.306	31.595	1.00	16.48	A	C
ATOM	1580	CB	ARG	A	516	18.842	8.134	31.882	1.00	17.00	A	C
ATOM	1583	CG	ARG	A	516	18.722	9.407	31.115	1.00	19.06	A	C
ATOM	1586	CD	ARG	A	516	17.815	10.406	31.760	1.00	18.75	A	C
ATOM	1589	NE	ARG	A	516	16.482	9.894	32.079	1.00	17.60	A	N
ATOM	1591	CZ	ARG	A	516	15.500	9.702	31.197	1.00	17.67	A	C
ATOM	1592	NH1	ARG	A	516	15.669	9.969	29.909	1.00	17.37	A	N
ATOM	1595	NH2	ARG	A	516	14.323	9.248	31.612	1.00	20.07	A	N
ATOM	1598	C	ARG	A	516	20.298	6.382	32.790	1.00	16.29	A	C
ATOM	1599	O	ARG	A	516	21.032	6.702	33.743	1.00	15.28	A	O
ATOM	1600	N	ASN	A	517	19.609	5.245	32.745	1.00	16.03	A	N
ATOM	1602	CA	ASN	A	517	19.387	4.432	33.927	1.00	15.86	A	C
ATOM	1604	CB	ASN	A	517	17.876	4.249	34.155	1.00	15.83	A	C
ATOM	1607	CG	ASN	A	517	17.161	5.562	34.430	1.00	16.01	A	C
ATOM	1608	OD1	ASN	A	517	16.182	5.918	33.758	1.00	16.60	A	O
ATOM	1609	ND2	ASN	A	517	17.671	6.316	35.390	1.00	15.03	A	N
ATOM	1612	C	ASN	A	517	20.108	3.092	33.863	1.00	16.06	A	C
ATOM	1613	O	ASN	A	517	19.900	2.238	34.715	1.00	15.77	A	O
ATOM	1614	N	LYS	A	518	20.980	2.928	32.870	1.00	16.16	A	N
ATOM	1616	CA	LYS	A	518	21.613	1.641	32.606	1.00	17.63	A	C
ATOM	1618	CB	LYS	A	518	22.643	1.784	31.474	1.00	17.77	A	C
ATOM	1621	CG	LYS	A	518	23.632	0.636	31.368	1.00	20.82	A	C
ATOM	1624	CD	LYS	A	518	24.421	0.686	30.063	1.00	24.15	A	C

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ATOM   1627  CE  LYS A 518      25.172   1.979  29.909  1.00 26.03      A    C
ATOM   1630  NZ  LYS A 518      24.304   3.106  29.435  1.00 28.18      A    N
ATOM   1634  C   LYS A 518      22.254   1.017  33.849  1.00 18.11      A    C
ATOM   1635  O   LYS A 518      22.126  -0.189  34.086  1.00 18.39      A    O
ATOM   1636  N   ASN A 519      22.938   1.825  34.652  1.00 18.49      A    N
ATOM   1638  CA  ASN A 519      23.671   1.287  35.802  1.00 19.30      A    C
ATOM   1640  CB  ASN A 519      24.611   2.346  36.375  1.00 19.86      A    C
ATOM   1643  CG  ASN A 519      25.664   2.759  35.382  1.00 21.38      A    C
ATOM   1644  OD1 ASN A 519      26.149   1.930  34.612  1.00 26.70      A    O
ATOM   1645  ND2 ASN A 519      26.012   4.042  35.372  1.00 28.25      A    N
ATOM   1648  C   ASN A 519      22.823   0.691  36.922  1.00 19.78      A    C
ATOM   1649  O   ASN A 519      23.344  -0.079  37.710  1.00 19.38      A    O
ATOM   1650  N   SER A 520      21.531   1.029  36.985  1.00 19.92      A    N
ATOM   1652  CA  SER A 520      20.647   0.503  38.031  1.00 20.71      A    C
ATOM   1654  CB  SER A 520      20.044   1.663  38.834  1.00 21.31      A    C
ATOM   1657  OG  SER A 520      19.120   2.400  38.069  1.00 23.80      A    O
ATOM   1659  C   SER A 520      19.536  -0.435  37.536  1.00 20.17      A    C
ATOM   1660  O   SER A 520      18.775  -0.953  38.335  1.00 21.79      A    O
ATOM   1661  N   LEU A 521      19.456  -0.678  36.234  1.00 18.62      A    N
ATOM   1663  CA  LEU A 521      18.417  -1.545  35.676  1.00 17.54      A    C
ATOM   1665  CB  LEU A 521      18.209  -1.218  34.192  1.00 17.30      A    C
ATOM   1668  CG  LEU A 521      17.417   0.046  33.909  1.00 17.34      A    C
ATOM   1670  CD1 LEU A 521      17.651   0.555  32.493  1.00 17.37      A    C
ATOM   1674  CD2 LEU A 521      15.950  -0.230  34.136  1.00 19.13      A    C
ATOM   1678  C   LEU A 521      18.794  -3.014  35.804  1.00 16.93      A    C
ATOM   1679  O   LEU A 521      19.938  -3.378  35.566  1.00 17.89      A    O
ATOM   1680  N   LYS A 522      17.841  -3.863  36.164  1.00 15.75      A    N
ATOM   1682  CA  LYS A 522      18.070  -5.314  36.231  1.00 15.93      A    C
ATOM   1684  CB  LYS A 522      17.277  -5.944  37.385  1.00 16.21      A    C
ATOM   1687  CG  LYS A 522      17.444  -5.237  38.719  1.00 18.79      A    C
ATOM   1690  CD  LYS A 522      16.528  -5.804  39.802  1.00 21.17      A    C
ATOM   1693  CE  LYS A 522      15.090  -5.353  39.648  1.00 23.90      A    C
ATOM   1696  NZ  LYS A 522      14.842  -3.888  39.964  1.00 25.89      A    N
ATOM   1700  C   LYS A 522      17.623  -5.956  34.915  1.00 14.75      A    C
ATOM   1701  O   LYS A 522      16.727  -5.432  34.257  1.00 14.52      A    O
ATOM   1702  N   VAL A 523      18.223  -7.096  34.556  1.00 13.60      A    N
ATOM   1704  CA  VAL A 523      17.821  -7.845  33.349  1.00 13.60      A    C
ATOM   1706  CB  VAL A 523      18.666  -9.113  33.137  1.00 13.75      A    C
ATOM   1708  CG1 VAL A 523      18.182  -9.891  31.939  1.00 13.84      A    C
ATOM   1712  CG2 VAL A 523      20.157  -8.741  32.968  1.00 14.55      A    C
ATOM   1716  C   VAL A 523      16.344  -8.238  33.420  1.00 13.39      A    C
ATOM   1717  O   VAL A 523      15.631  -8.222  32.427  1.00 12.33      A    O
ATOM   1718  N   LEU A 524      15.887  -8.535  34.626  1.00 13.26      A    N
ATOM   1720  CA  LEU A 524      14.512  -8.886  34.875  1.00 14.13      A    C
ATOM   1722  CB  LEU A 524      14.392  -9.107  36.382  1.00 15.52      A    C
ATOM   1725  CG  LEU A 524      13.090  -9.468  37.032  1.00 20.72      A    C
ATOM   1727  CD1 LEU A 524      12.523 -10.698  36.358  1.00 22.55      A    C
ATOM   1731  CD2 LEU A 524      13.407  -9.706  38.518  1.00 22.42      A    C
ATOM   1735  C   LEU A 524      13.556  -7.804  34.362  1.00 12.61      A    C
ATOM   1736  O   LEU A 524      12.528  -8.109  33.738  1.00 11.66      A    O
ATOM   1737  N   THR A 525      13.909  -6.544  34.590  1.00 11.21      A    N
ATOM   1739  CA  THR A 525      13.113  -5.402  34.123  1.00 11.25      A    C
ATOM   1741  CB  THR A 525      13.650  -4.120  34.788  1.00 11.51      A    C
ATOM   1743  OG1 THR A 525      13.552  -4.260  36.215  1.00 13.76      A    O
ATOM   1745  CG2 THR A 525      12.815  -2.922  34.467  1.00 11.96      A    C
ATOM   1749  C   THR A 525      13.124  -5.235  32.600  1.00 10.93      A    C
ATOM   1750  O   THR A 525      12.114  -4.850  32.001  1.00 10.34      A    O
ATOM   1751  N   LEU A 526      14.275  -5.482  31.987  1.00  9.76      A    N
ATOM   1753  CA  LEU A 526      14.412  -5.405  30.523  1.00  9.91      A    C
ATOM   1755  CB  LEU A 526      15.877  -5.597  30.105  1.00  9.71      A    C
ATOM   1758  CG  LEU A 526      16.878  -4.621  30.717  1.00 10.00      A    C
ATOM   1760  CD1 LEU A 526      18.268  -4.904  30.219  1.00 10.63      A    C
ATOM   1764  CD2 LEU A 526      16.484  -3.208  30.422  1.00 10.98      A    C
ATOM   1768  C   LEU A 526      13.520  -6.455  29.836  1.00  9.82      A    C
ATOM   1769  O   LEU A 526      12.876  -6.176  28.822  1.00  8.11      A    O
ATOM   1770  N   VAL A 527      13.475  -7.660  30.411  1.00  9.84      A    N
ATOM   1772  CA  VAL A 527      12.588  -8.709  29.924  1.00 10.01      A    C
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ATOM	1774	CB	VAL	A	527	12.910	-10.075	30.588	1.00	10.28	A	C
ATOM	1776	CG1	VAL	A	527	11.950	-11.157	30.103	1.00	12.12	A	C
ATOM	1780	CG2	VAL	A	527	14.326	-10.464	30.275	1.00	11.61	A	C
ATOM	1784	C	VAL	A	527	11.111	-8.316	30.132	1.00	9.91	A	C
ATOM	1785	O	VAL	A	527	10.286	-8.533	29.247	1.00	9.20	A	O
ATOM	1786	N	LEU	A	528	10.783	-7.715	31.277	1.00	9.17	A	N
ATOM	1788	CA	LEU	A	528	9.419	-7.239	31.548	1.00	9.55	A	C
ATOM	1790	CB	LEU	A	528	9.308	-6.582	32.940	1.00	10.47	A	C
ATOM	1793	CG	LEU	A	528	7.962	-5.908	33.230	1.00	11.24	A	C
ATOM	1795	CD1	LEU	A	528	6.855	-6.956	33.158	1.00	11.66	A	C
ATOM	1799	CD2	LEU	A	528	7.961	-5.179	34.544	1.00	12.72	A	C
ATOM	1803	C	LEU	A	528	8.976	-6.263	30.464	1.00	9.67	A	C
ATOM	1804	O	LEU	A	528	7.878	-6.389	29.928	1.00	8.64	A	O
ATOM	1805	N	TYR	A	529	9.825	-5.290	30.120	1.00	9.08	A	N
ATOM	1807	CA	TYR	A	529	9.447	-4.301	29.091	1.00	8.78	A	C
ATOM	1809	CB	TYR	A	529	10.522	-3.215	28.939	1.00	8.57	A	C
ATOM	1812	CG	TYR	A	529	10.744	-2.321	30.143	1.00	10.12	A	C
ATOM	1813	CD1	TYR	A	529	9.833	-2.257	31.193	1.00	10.85	A	C
ATOM	1815	CE1	TYR	A	529	10.057	-1.438	32.298	1.00	12.11	A	C
ATOM	1817	CZ	TYR	A	529	11.211	-0.677	32.365	1.00	13.84	A	C
ATOM	1818	OH	TYR	A	529	11.441	0.140	33.449	1.00	16.48	A	O
ATOM	1820	CE2	TYR	A	529	12.137	-0.737	31.354	1.00	11.18	A	C
ATOM	1822	CD2	TYR	A	529	11.903	-1.565	30.248	1.00	11.83	A	C
ATOM	1824	C	TYR	A	529	9.202	-4.967	27.734	1.00	8.22	A	C
ATOM	1825	O	TYR	A	529	8.255	-4.615	27.028	1.00	9.04	A	O
ATOM	1826	N	SER	A	530	10.036	-5.937	27.390	1.00	8.24	A	N
ATOM	1828	CA	SER	A	530	9.889	-6.722	26.154	1.00	7.83	A	C
ATOM	1830	CB	SER	A	530	11.052	-7.730	26.015	1.00	7.54	A	C
ATOM	1833	OG	SER	A	530	12.310	-7.077	25.839	1.00	10.28	A	O
ATOM	1835	C	SER	A	530	8.543	-7.458	26.137	1.00	7.48	A	C
ATOM	1836	O	SER	A	530	7.820	-7.443	25.141	1.00	7.17	A	O
ATOM	1837	N	LEU	A	531	8.199	-8.074	27.258	1.00	6.73	A	N
ATOM	1839	CA	LEU	A	531	6.931	-8.800	27.389	1.00	7.75	A	C
ATOM	1841	CB	LEU	A	531	6.912	-9.561	28.728	1.00	7.60	A	C
ATOM	1844	CG	LEU	A	531	5.618	-10.232	29.178	1.00	8.41	A	C
ATOM	1846	CD1	LEU	A	531	5.201	-11.263	28.153	1.00	9.01	A	C
ATOM	1850	CD2	LEU	A	531	5.776	-10.881	30.561	1.00	11.57	A	C
ATOM	1854	C	LEU	A	531	5.731	-7.876	27.280	1.00	7.08	A	C
ATOM	1855	O	LEU	A	531	4.745	-8.201	26.644	1.00	6.97	A	O
ATOM	1856	N	GLN	A	532	5.797	-6.711	27.911	1.00	7.33	A	N
ATOM	1858	CA	GLN	A	532	4.706	-5.735	27.831	1.00	7.02	A	C
ATOM	1860	CB	GLN	A	532	5.050	-4.514	28.702	1.00	6.93	A	C
ATOM	1863	CG	GLN	A	532	4.930	-4.815	30.195	1.00	7.50	A	C
ATOM	1866	CD	GLN	A	532	5.235	-3.632	31.101	1.00	9.98	A	C
ATOM	1867	OE1	GLN	A	532	5.756	-2.626	30.657	1.00	9.61	A	O
ATOM	1868	NE2	GLN	A	532	4.903	-3.772	32.393	1.00	8.99	A	N
ATOM	1871	C	GLN	A	532	4.439	-5.290	26.388	1.00	7.09	A	C
ATOM	1872	O	GLN	A	532	3.281	-5.223	25.942	1.00	6.73	A	O
ATOM	1873	N	ILE	A	533	5.505	-4.991	25.645	1.00	7.80	A	N
ATOM	1875	CA	ILE	A	533	5.341	-4.572	24.264	1.00	8.29	A	C
ATOM	1877	CB	ILE	A	533	6.663	-4.028	23.692	1.00	8.97	A	C
ATOM	1879	CG1	ILE	A	533	7.124	-2.779	24.445	1.00	8.38	A	C
ATOM	1882	CD1	ILE	A	533	6.158	-1.630	24.424	1.00	9.69	A	C
ATOM	1886	CG2	ILE	A	533	6.527	-3.760	22.221	1.00	9.41	A	C
ATOM	1890	C	ILE	A	533	4.825	-5.736	23.419	1.00	8.33	A	C
ATOM	1891	O	ILE	A	533	4.010	-5.548	22.512	1.00	8.38	A	O
ATOM	1892	N	CYS	A	534	5.305	-6.938	23.717	1.00	7.80	A	N
ATOM	1894	CA	CYS	A	534	4.829	-8.141	23.044	1.00	8.73	A	C
ATOM	1896	CB	CYS	A	534	5.588	-9.373	23.521	1.00	9.35	A	C
ATOM	1899	SG	CYS	A	534	5.440	-10.785	22.388	1.00	10.44	A	S
ATOM	1900	C	CYS	A	534	3.332	-8.326	23.234	1.00	8.30	A	C
ATOM	1901	O	CYS	A	534	2.638	-8.690	22.279	1.00	7.97	A	O
ATOM	1902	N	LYS	A	535	2.821	-8.083	24.451	1.00	8.09	A	N
ATOM	1904	CA	LYS	A	535	1.381	-8.179	24.685	1.00	8.26	A	C
ATOM	1906	CB	LYS	A	535	1.055	-8.053	26.169	1.00	8.37	A	C
ATOM	1909	CG	LYS	A	535	1.491	-9.239	26.965	1.00	10.48	A	C
ATOM	1912	CD	LYS	A	535	1.166	-9.072	28.438	1.00	13.12	A	C

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ATOM   1915  CE  LYS A 535       1.380 -10.378  29.159  1.00 15.75      A    C
ATOM   1918  NZ  LYS A 535       1.022 -10.255  30.588  1.00 19.99      A    N
ATOM   1922  C   LYS A 535       0.569  -7.160  23.880  1.00  8.96      A    C
ATOM   1923  O   LYS A 535      -0.525  -7.471  23.383  1.00  8.89      A    O
ATOM   1924  N   ALA A 536       1.079  -5.946  23.758  1.00  8.31      A    N
ATOM   1926  CA  ALA A 536       0.461  -4.964  22.870  1.00  8.35      A    C
ATOM   1928  CB  ALA A 536       1.208  -3.652  22.932  1.00  8.92      A    C
ATOM   1932  C   ALA A 536       0.418  -5.463  21.434  1.00  8.28      A    C
ATOM   1933  O   ALA A 536      -0.595  -5.288  20.745  1.00  8.64      A    O
ATOM   1934  N   MET A 537       1.505  -6.073  20.973  1.00  7.09      A    N
ATOM   1936  CA  MET A 537       1.578  -6.552  19.596  1.00  7.42      A    C
ATOM   1938  CB  MET A 537       3.020  -6.875  19.183  1.00  7.57      A    C
ATOM   1941  CG  MET A 537       3.879  -5.632  19.008  1.00  7.90      A    C
ATOM   1944  SD  MET A 537       3.169  -4.342  17.962  1.00 11.76      A    S
ATOM   1945  CE  MET A 537       2.724  -5.210  16.517  1.00 14.61      A    C
ATOM   1949  C   MET A 537       0.679  -7.755  19.365  1.00  7.65      A    C
ATOM   1950  O   MET A 537       0.122  -7.907  18.271  1.00  8.38      A    O
ATOM   1951  N   ALA A 538       0.479  -8.576  20.386  1.00  7.79      A    N
ATOM   1953  CA  ALA A 538      -0.451  -9.717  20.244  1.00  8.20      A    C
ATOM   1955  CB  ALA A 538      -0.415 -10.622  21.450  1.00  8.47      A    C
ATOM   1959  C   ALA A 538      -1.876  -9.203  20.011  1.00  8.12      A    C
ATOM   1960  O   ALA A 538      -2.643  -9.800  19.251  1.00  8.25      A    O
ATOM   1961  N   TYR A 539      -2.230  -8.116  20.670  1.00  8.11      A    N
ATOM   1963  CA  TYR A 539      -3.542  -7.483  20.457  1.00  9.32      A    C
ATOM   1965  CB  TYR A 539      -3.774  -6.365  21.469  1.00  9.99      A    C
ATOM   1968  CG  TYR A 539      -5.068  -5.630  21.207  1.00 11.93      A    C
ATOM   1969  CD1 TYR A 539      -6.271  -6.313  21.198  1.00 15.15      A    C
ATOM   1971  CE1 TYR A 539      -7.490  -5.653  20.916  1.00 19.59      A    C
ATOM   1973  CZ  TYR A 539      -7.490  -4.300  20.654  1.00 21.53      A    C
ATOM   1974  OH  TYR A 539      -8.702  -3.667  20.376  1.00 25.74      A    O
ATOM   1976  CE2 TYR A 539      -6.300  -3.595  20.656  1.00 19.80      A    C
ATOM   1978  CD2 TYR A 539      -5.082  -4.267  20.928  1.00 17.80      A    C
ATOM   1980  C   TYR A 539      -3.671  -6.953  19.013  1.00  9.25      A    C
ATOM   1981  O   TYR A 539      -4.671  -7.228  18.327  1.00 10.22      A    O
ATOM   1982  N   LEU A 540      -2.662  -6.226  18.534  1.00  8.68      A    N
ATOM   1984  CA  LEU A 540      -2.681  -5.747  17.162  1.00  9.52      A    C
ATOM   1986  CB  LEU A 540      -1.497  -4.781  16.902  1.00  9.52      A    C
ATOM   1989  CG  LEU A 540      -1.503  -3.503  17.757  1.00  9.17      A    C
ATOM   1991  CD1 LEU A 540      -0.301  -2.603  17.427  1.00 12.37      A    C
ATOM   1995  CD2 LEU A 540      -2.795  -2.746  17.652  1.00 11.42      A    C
ATOM   1999  C   LEU A 540      -2.765  -6.896  16.132  1.00 10.02      A    C
ATOM   2000  O   LEU A 540      -3.496  -6.801  15.139  1.00 10.77      A    O
ATOM   2001  N   GLU A 541      -2.053  -7.983  16.386  1.00  9.88      A    N
ATOM   2003  CA  GLU A 541      -2.071  -9.173  15.534  1.00 10.37      A    C
ATOM   2005  CB  GLU A 541      -1.081 -10.216  16.087  1.00 10.24      A    C
ATOM   2008  CG  GLU A 541      -1.140 -11.612  15.478  1.00 11.36      A    C
ATOM   2011  CD  GLU A 541      -0.136 -12.569  16.101  1.00 10.66      A    C
ATOM   2012  OE1 GLU A 541      -0.448 -13.191  17.153  1.00 11.76      A    O
ATOM   2013  OE2 GLU A 541       0.968 -12.704  15.543  1.00 11.66      A    O
ATOM   2014  C   GLU A 541      -3.491  -9.739  15.437  1.00 10.85      A    C
ATOM   2015  O   GLU A 541      -3.907 -10.192  14.378  1.00 11.81      A    O
ATOM   2016  N   SER A 542      -4.243  -9.677  16.531  1.00 11.36      A    N
ATOM   2018  CA  SER A 542      -5.608 -10.206  16.550  1.00 11.65      A    C
ATOM   2020  CB  SER A 542      -6.160 -10.250  17.976  1.00 12.06      A    C
ATOM   2023  OG  SER A 542      -6.549  -8.983  18.468  1.00 11.97      A    O
ATOM   2025  C   SER A 542      -6.576  -9.458  15.641  1.00 12.56      A    C
ATOM   2026  O   SER A 542      -7.631 -10.010  15.277  1.00 11.49      A    O
ATOM   2027  N   ILE A 543      -6.260  -8.210  15.323  1.00 12.89      A    N
ATOM   2029  CA  ILE A 543      -7.050  -7.424  14.358  1.00 13.67      A    C
ATOM   2031  CB  ILE A 543      -7.562  -6.115  14.994  1.00 14.02      A    C
ATOM   2033  CG1 ILE A 543      -6.433  -5.283  15.598  1.00 14.22      A    C
ATOM   2036  CD1 ILE A 543      -6.826  -3.900  15.926  1.00 15.54      A    C
ATOM   2040  CG2 ILE A 543      -8.591  -6.404  16.074  1.00 13.84      A    C
ATOM   2044  C   ILE A 543      -6.317  -7.159  13.042  1.00 14.47      A    C
ATOM   2045  O   ILE A 543      -6.732  -6.316  12.252  1.00 14.15      A    O
ATOM   2046  N   ASN A 544      -5.235  -7.885  12.809  1.00 15.25      A    N
ATOM   2048  CA  ASN A 544      -4.457  -7.780  11.575  1.00 17.01      A    C
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ATOM   2050  CB  ASN A 544      -5.260  -8.311  10.368  1.00 18.38      A    C
ATOM   2053  CG  ASN A 544      -5.668  -9.758  10.523  1.00 22.26      A    C
ATOM   2054  OD1 ASN A 544      -4.821 -10.644  10.660  1.00 28.79      A    O
ATOM   2055  ND2 ASN A 544      -6.970 -10.012  10.491  1.00 27.53      A    N
ATOM   2058  C   ASN A 544      -3.995  -6.353  11.302  1.00 17.05      A    C
ATOM   2059  O   ASN A 544      -4.019  -5.878  10.162  1.00 18.03      A    O
ATOM   2060  N   CYS A 545      -3.591  -5.672  12.365  1.00 16.00      A    N
ATOM   2062  CA  CYS A 545      -3.103  -4.305  12.291  1.00 16.72      A    C
ATOM   2064  CB  CYS A 545      -3.628  -3.544  13.494  1.00 16.76      A    C
ATOM   2067  SG  CYS A 545      -3.019  -1.887  13.701  1.00 24.49      A    S
ATOM   2068  C   CYS A 545      -1.586  -4.358  12.295  1.00 15.33      A    C
ATOM   2069  O   CYS A 545      -0.994  -4.800  13.278  1.00 15.78      A    O
ATOM   2070  N   VAL A 546      -0.969  -3.933  11.194  1.00 14.28      A    N
ATOM   2072  CA  VAL A 546       0.498  -3.913  11.064  1.00 13.55      A    C
ATOM   2074  CB  VAL A 546       0.939  -4.206   9.610  1.00 14.14      A    C
ATOM   2076  CG1 VAL A 546       2.466  -4.261   9.507  1.00 15.81      A    C
ATOM   2080  CG2 VAL A 546       0.296  -5.520   9.111  1.00 15.91      A    C
ATOM   2084  C   VAL A 546       0.998  -2.542  11.524  1.00 13.04      A    C
ATOM   2085  O   VAL A 546       0.606  -1.505  10.980  1.00 12.91      A    O
ATOM   2086  N   HIS A 547       1.871  -2.540  12.533  1.00 11.11      A    N
ATOM   2088  CA  HIS A 547       2.287  -1.318  13.227  1.00 10.91      A    C
ATOM   2090  CB  HIS A 547       2.643  -1.668  14.683  1.00 10.19      A    C
ATOM   2093  CG  HIS A 547       2.902  -0.475  15.544  1.00 10.34      A    C
ATOM   2094  ND1 HIS A 547       4.081   0.228  15.491  1.00 11.48      A    N
ATOM   2096  CE1 HIS A 547       4.038   1.226  16.361  1.00 10.70      A    C
ATOM   2098  NE2 HIS A 547       2.864   1.199  16.967  1.00  9.34      A    N
ATOM   2100  CD2 HIS A 547       2.140   0.138  16.481  1.00 10.35      A    C
ATOM   2102  C   HIS A 547       3.431  -0.584  12.527  1.00 10.89      A    C
ATOM   2103  O   HIS A 547       3.342   0.628  12.322  1.00 11.28      A    O
ATOM   2104  N   ARG A 548       4.479  -1.321  12.157  1.00 10.62      A    N
ATOM   2106  CA  ARG A 548       5.652  -0.819  11.406  1.00 10.76      A    C
ATOM   2108  CB  ARG A 548       5.248  -0.092  10.114  1.00 11.42      A    C
ATOM   2111  CG  ARG A 548       4.346  -0.845   9.128  1.00 12.89      A    C
ATOM   2114  CD  ARG A 548       4.246  -0.093   7.781  1.00 15.96      A    C
ATOM   2117  NE  ARG A 548       3.297  -0.686   6.841  1.00 16.19      A    N
ATOM   2119  CZ  ARG A 548       3.236  -0.367   5.543  1.00 18.71      A    C
ATOM   2120  NH1 ARG A 548       4.045   0.549   5.039  1.00 17.01      A    N
ATOM   2123  NH2 ARG A 548       2.350  -0.948   4.752  1.00 19.52      A    N
ATOM   2126  C   ARG A 548       6.616   0.100  12.165  1.00 10.94      A    C
ATOM   2127  O   ARG A 548       7.610   0.540  11.585  1.00 11.17      A    O
ATOM   2128  N   ASP A 549       6.345   0.423  13.421  1.00 10.64      A    N
ATOM   2130  CA  ASP A 549       7.255   1.294  14.181  1.00 11.41      A    C
ATOM   2132  CB  ASP A 549       6.824   2.767  14.120  1.00 11.59      A    C
ATOM   2135  CG  ASP A 549       7.947   3.735  14.497  1.00 16.46      A    C
ATOM   2136  OD1 ASP A 549       9.129   3.319  14.543  1.00 19.23      A    O
ATOM   2137  OD2 ASP A 549       7.726   4.944  14.778  1.00 18.02      A    O
ATOM   2138  C   ASP A 549       7.456   0.836  15.616  1.00 10.41      A    C
ATOM   2139  O   ASP A 549       7.269   1.597  16.576  1.00 10.29      A    O
ATOM   2140  N   ILE A 550       7.926  -0.400  15.743  1.00 10.29      A    N
ATOM   2142  CA  ILE A 550       8.229  -0.986  17.046  1.00 10.14      A    C
ATOM   2144  CB  ILE A 550       7.858  -2.490  17.037  1.00 10.18      A    C
ATOM   2146  CG1 ILE A 550       6.440  -2.685  16.476  1.00  9.59      A    C
ATOM   2149  CD1 ILE A 550       6.199  -4.070  15.917  1.00 12.93      A    C
ATOM   2153  CG2 ILE A 550       7.936  -3.059  18.435  1.00 10.80      A    C
ATOM   2157  C   ILE A 550       9.709  -0.791  17.310  1.00 10.07      A    C
ATOM   2158  O   ILE A 550      10.517  -1.517  16.793  1.00 10.23      A    O
ATOM   2159  N   ALA A 551      10.032   0.227  18.094  1.00 10.23      A    N
ATOM   2161  CA  ALA A 551      11.403   0.671  18.312  1.00  9.79      A    C
ATOM   2163  CB  ALA A 551      11.883   1.526  17.130  1.00  9.99      A    C
ATOM   2167  C   ALA A 551      11.404   1.495  19.593  1.00  9.51      A    C
ATOM   2168  O   ALA A 551      10.399   2.111  19.911  1.00  8.53      A    O
ATOM   2169  N   VAL A 552      12.536   1.529  20.304  1.00  8.79      A    N
ATOM   2171  CA  VAL A 552      12.595   2.169  21.630  1.00  9.71      A    C
ATOM   2173  CB  VAL A 552      13.917   1.852  22.434  1.00  9.32      A    C
ATOM   2175  CG1 VAL A 552      13.981   0.377  22.814  1.00 11.97      A    C
ATOM   2179  CG2 VAL A 552      15.175   2.296  21.700  1.00 10.51      A    C
ATOM   2183  C   VAL A 552      12.373   3.671  21.605  1.00  9.86      A    C
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ATOM   2184  O   VAL A 552      11.910   4.231  22.605  1.00  9.34      A    O
ATOM   2185  N   ARG A 553      12.672   4.305  20.462  1.00  9.93      A    N
ATOM   2187  CA  ARG A 553      12.381   5.715  20.233  1.00 11.22      A    C
ATOM   2189  CB  ARG A 553      12.914   6.152  18.849  1.00 12.32      A    C
ATOM   2192  CG  ARG A 553      12.746   7.598  18.520  1.00 18.30      A    C
ATOM   2195  CD  ARG A 553      13.541   8.051  17.284  1.00 25.13      A    C
ATOM   2198  NE  ARG A 553      13.202   9.422  16.907  1.00 30.79      A    N
ATOM   2200  CZ  ARG A 553      13.974  10.246  16.190  1.00 34.09      A    C
ATOM   2201  NH1 ARG A 553      15.161   9.865  15.721  1.00 35.69      A    N
ATOM   2204  NH2 ARG A 553      13.536  11.475  15.928  1.00 35.84      A    N
ATOM   2207  C   ARG A 553      10.873   5.962  20.295  1.00 10.85      A    C
ATOM   2208  O   ARG A 553      10.427   7.061  20.646  1.00  9.83      A    O
ATOM   2209  N   ASN A 554      10.101   4.948  19.911  1.00  8.85      A    N
ATOM   2211  CA  ASN A 554       8.650   5.050  19.820  1.00  9.54      A    C
ATOM   2213  CB  ASN A 554       8.173   4.595  18.434  1.00  8.92      A    C
ATOM   2216  CG  ASN A 554       6.729   4.998  18.148  1.00 10.60      A    C
ATOM   2217  OD1 ASN A 554       6.321   6.131  18.457  1.00 11.60      A    O
ATOM   2218  ND2 ASN A 554       5.959   4.101  17.560  1.00 11.34      A    N
ATOM   2221  C   ASN A 554       7.907   4.279  20.910  1.00  9.30      A    C
ATOM   2222  O   ASN A 554       6.788   3.841  20.707  1.00 10.60      A    O
ATOM   2223  N   ILE A 555       8.544   4.108  22.062  1.00 10.21      A    N
ATOM   2225  CA  ILE A 555       7.935   3.514  23.235  1.00  9.86      A    C
ATOM   2227  CB  ILE A 555       8.595   2.177  23.597  1.00  9.61      A    C
ATOM   2229  CG1 ILE A 555       8.358   1.140  22.488  1.00 10.41      A    C
ATOM   2232  CD1 ILE A 555       9.318   0.017  22.555  1.00 11.60      A    C
ATOM   2236  CG2 ILE A 555       8.103   1.672  24.948  1.00  9.20      A    C
ATOM   2240  C   ILE A 555       8.114   4.536  24.350  1.00 10.75      A    C
ATOM   2241  O   ILE A 555       9.208   5.071  24.541  1.00 10.55      A    O
ATOM   2242  N   LEU A 556       7.044   4.807  25.088  1.00 10.73      A    N
ATOM   2244  CA  LEU A 556       7.084   5.751  26.209  1.00 11.14      A    C
ATOM   2246  CB  LEU A 556       5.932   6.765  26.100  1.00 11.83      A    C
ATOM   2249  CG  LEU A 556       6.005   7.814  24.986  1.00 14.83      A    C
ATOM   2251  CD1 LEU A 556       7.308   8.567  24.986  1.00 18.18      A    C
ATOM   2255  CD2 LEU A 556       5.770   7.191  23.644  1.00 19.54      A    C
ATOM   2259  C   LEU A 556       7.001   5.052  27.535  1.00 10.30      A    C
ATOM   2260  O   LEU A 556       6.353   4.017  27.670  1.00  9.91      A    O
ATOM   2261  N   VAL A 557       7.636   5.660  28.529  1.00  9.82      A    N
ATOM   2263  CA  VAL A 557       7.790   5.088  29.856  1.00 10.20      A    C
ATOM   2265  CB  VAL A 557       9.244   5.235  30.379  1.00  9.42      A    C
ATOM   2267  CG1 VAL A 557       9.382   4.662  31.776  1.00  9.30      A    C
ATOM   2271  CG2 VAL A 557      10.274   4.537  29.435  1.00 10.82      A    C
ATOM   2275  C   VAL A 557       6.809   5.808  30.788  1.00 10.92      A    C
ATOM   2276  O   VAL A 557       6.990   6.979  31.126  1.00 10.29      A    O
ATOM   2277  N   ALA A 558       5.744   5.103  31.149  1.00 11.83      A    N
ATOM   2279  CA  ALA A 558       4.753   5.595  32.116  1.00 12.73      A    C
ATOM   2281  CB  ALA A 558       3.474   4.716  32.040  1.00 12.91      A    C
ATOM   2285  C   ALA A 558       5.291   5.615  33.542  1.00 13.27      A    C
ATOM   2286  O   ALA A 558       5.043   6.550  34.330  1.00 14.71      A    O
ATOM   2287  N   SER A 559       6.010   4.559  33.884  1.00 13.11      A    N
ATOM   2289  CA  SER A 559       6.639   4.396  35.186  1.00 13.68      A    C
ATOM   2291  CB  SER A 559       5.618   3.934  36.220  1.00 13.21      A    C
ATOM   2294  OG  SER A 559       5.230   2.589  36.006  1.00 13.73      A    O
ATOM   2296  C   SER A 559       7.719   3.352  35.030  1.00 13.54      A    C
ATOM   2297  O   SER A 559       7.737   2.663  34.025  1.00 12.55      A    O
ATOM   2298  N   PRO A 560       8.593   3.177  36.018  1.00 14.61      A    N
ATOM   2299  CA  PRO A 560       9.559   2.069  35.950  1.00 15.41      A    C
ATOM   2301  CB  PRO A 560      10.361   2.217  37.251  1.00 15.46      A    C
ATOM   2304  CG  PRO A 560      10.251   3.662  37.572  1.00 15.49      A    C
ATOM   2307  CD  PRO A 560       8.794   3.996  37.233  1.00 15.51      A    C
ATOM   2310  C   PRO A 560       8.919   0.678  35.800  1.00 15.83      A    C
ATOM   2311  O   PRO A 560       9.589  -0.279  35.390  1.00 16.34      A    O
ATOM   2312  N   GLU A 561       7.626   0.579  36.070  1.00 16.53      A    N
ATOM   2314  CA  GLU A 561       6.918  -0.689  35.993  1.00 16.63      A    C
ATOM   2316  CB  GLU A 561       6.035  -0.834  37.234  1.00 18.01      A    C
ATOM   2319  CG  GLU A 561       6.833  -0.946  38.529  1.00 22.37      A    C
ATOM   2322  CD  GLU A 561       6.517   0.168  39.506  1.00 28.24      A    C
ATOM   2323  OE1 GLU A 561       6.453   1.357  39.072  1.00 32.07      A    O
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ATOM	2324	OE2	GLU	A	561	6.315	-0.152	40.707	1.00	33.30	A	O
ATOM	2325	C	GLU	A	561	6.059	-0.871	34.733	1.00	14.93	A	C
ATOM	2326	O	GLU	A	561	5.445	-1.916	34.574	1.00	14.59	A	O
ATOM	2327	N	CYS	A	562	6.025	0.111	33.835	1.00	13.75	A	N
ATOM	2329	CA	CYS	A	562	5.074	0.089	32.711	1.00	14.08	A	C
ATOM	2331	CB	CYS	A	562	3.692	0.541	33.159	1.00	14.16	A	C
ATOM	2334	SG	CYS	A	562	2.464	0.485	31.846	1.00	17.94	A	S
ATOM	2335	C	CYS	A	562	5.534	0.942	31.520	1.00	12.60	A	C
ATOM	2336	O	CYS	A	562	5.747	2.155	31.640	1.00	12.45	A	O
ATOM	2337	N	VAL	A	563	5.709	0.282	30.377	1.00	11.25	A	N
ATOM	2339	CA	VAL	A	563	5.979	0.962	29.125	1.00	10.38	A	C
ATOM	2341	CB	VAL	A	563	7.259	0.421	28.421	1.00	10.60	A	C
ATOM	2343	CG1	VAL	A	563	8.477	0.548	29.329	1.00	10.27	A	C
ATOM	2347	CG2	VAL	A	563	7.102	-1.020	27.949	1.00	10.55	A	C
ATOM	2351	C	VAL	A	563	4.748	0.912	28.184	1.00	10.67	A	C
ATOM	2352	O	VAL	A	563	3.867	0.058	28.336	1.00	10.13	A	O
ATOM	2353	N	LYS	A	564	4.723	1.806	27.202	1.00	9.96	A	N
ATOM	2355	CA	LYS	A	564	3.586	1.997	26.285	1.00	10.71	A	C
ATOM	2357	CB	LYS	A	564	2.835	3.290	26.642	1.00	10.90	A	C
ATOM	2360	CG	LYS	A	564	2.453	3.420	28.104	1.00	13.45	A	C
ATOM	2363	CD	LYS	A	564	1.102	2.850	28.403	1.00	14.37	A	C
ATOM	2366	CE	LYS	A	564	0.676	3.158	29.838	1.00	16.32	A	C
ATOM	2369	NZ	LYS	A	564	-0.589	2.458	30.221	1.00	17.26	A	N
ATOM	2373	C	LYS	A	564	4.050	2.148	24.828	1.00	9.71	A	C
ATOM	2374	O	LYS	A	564	4.814	3.069	24.502	1.00	9.88	A	O
ATOM	2375	N	LEU	A	565	3.615	1.238	23.964	1.00	8.95	A	N
ATOM	2377	CA	LEU	A	565	3.909	1.334	22.533	1.00	9.28	A	C
ATOM	2379	CB	LEU	A	565	3.418	0.094	21.802	1.00	9.45	A	C
ATOM	2382	CG	LEU	A	565	3.702	0.004	20.289	1.00	9.53	A	C
ATOM	2384	CD1	LEU	A	565	5.202	0.062	20.003	1.00	10.72	A	C
ATOM	2388	CD2	LEU	A	565	3.070	-1.258	19.781	1.00	12.45	A	C
ATOM	2392	C	LEU	A	565	3.245	2.565	21.928	1.00	9.46	A	C
ATOM	2393	O	LEU	A	565	2.054	2.825	22.167	1.00	9.53	A	O
ATOM	2394	N	GLY	A	566	4.007	3.302	21.131	1.00	10.94	A	N
ATOM	2396	CA	GLY	A	566	3.540	4.539	20.511	1.00	12.38	A	C
ATOM	2399	C	GLY	A	566	2.748	4.337	19.222	1.00	14.40	A	C
ATOM	2400	O	GLY	A	566	2.312	3.235	18.882	1.00	12.68	A	O
ATOM	2401	N	ASP	A	567	2.524	5.424	18.494	1.00	17.06	A	N
ATOM	2403	CA	ASP	A	567	1.644	5.322	17.327	1.00	19.73	A	C
ATOM	2405	CB	ASP	A	567	0.986	6.649	16.942	1.00	21.13	A	C
ATOM	2408	CG	ASP	A	567	1.917	7.779	16.889	1.00	24.80	A	C
ATOM	2409	OD1	ASP	A	567	2.981	7.672	16.231	1.00	32.54	A	O
ATOM	2410	OD2	ASP	A	567	1.623	8.856	17.439	1.00	29.95	A	O
ATOM	2411	C	ASP	A	567	2.257	4.622	16.108	1.00	20.41	A	C
ATOM	2412	O	ASP	A	567	3.467	4.413	16.011	1.00	17.31	A	O
ATOM	2413	N	PHE	A	568	1.368	4.262	15.196	1.00	22.78	A	N
ATOM	2415	CA	PHE	A	568	1.698	3.525	13.979	1.00	25.32	A	C
ATOM	2417	CB	PHE	A	568	0.428	3.274	13.152	1.00	26.08	A	C
ATOM	2420	CG	PHE	A	568	-0.619	2.555	13.894	1.00	27.54	A	C
ATOM	2421	CD1	PHE	A	568	-1.780	3.199	14.285	1.00	29.54	A	C
ATOM	2423	CE1	PHE	A	568	-2.745	2.522	14.983	1.00	29.57	A	C
ATOM	2425	CZ	PHE	A	568	-2.560	1.197	15.312	1.00	30.42	A	C
ATOM	2427	CE2	PHE	A	568	-1.412	0.548	14.935	1.00	30.12	A	C
ATOM	2429	CD2	PHE	A	568	-0.443	1.228	14.228	1.00	29.43	A	C
ATOM	2431	C	PHE	A	568	2.666	4.282	13.116	1.00	27.26	A	C
ATOM	2432	O	PHE	A	568	2.610	5.502	13.050	1.00	27.24	A	O
ATOM	2433	N	GLY	A	569	3.536	3.545	12.433	1.00	29.69	A	N
ATOM	2435	CA	GLY	A	569	4.511	4.124	11.531	1.00	32.08	A	C
ATOM	2438	C	GLY	A	569	3.937	5.058	10.482	1.00	34.61	A	C
ATOM	2439	O	GLY	A	569	4.602	6.029	10.110	1.00	34.79	A	O
ATOM	2440	N	LEU	A	570	2.724	4.754	10.010	1.00	37.79	A	N
ATOM	2442	CA	LEU	A	570	1.999	5.549	8.993	1.00	40.50	A	C
ATOM	2444	CB	LEU	A	570	0.514	5.665	9.387	1.00	40.83	A	C
ATOM	2447	CG	LEU	A	570	-0.463	6.442	8.489	1.00	41.93	A	C
ATOM	2449	CD1	LEU	A	570	-0.487	5.925	7.051	1.00	42.79	A	C
ATOM	2453	CD2	LEU	A	570	-1.870	6.383	9.095	1.00	42.81	A	C
ATOM	2457	C	LEU	A	570	2.572	6.949	8.737	1.00	42.14	A	C

ATOM	2458	O	LEU	A	570	2.682	7.769	9.670	1.00	43.08	A	O
ATOM	2459	N	SER	A	571	2.929	7.207	7.475	1.00	43.89	A	N
ATOM	2461	CA	SER	A	571	3.588	8.455	7.062	1.00	45.06	A	C
ATOM	2463	CB	SER	A	571	4.686	8.163	6.017	1.00	45.02	A	C
ATOM	2466	OG	SER	A	571	5.526	7.091	6.423	1.00	45.78	A	O
ATOM	2468	C	SER	A	571	2.551	9.456	6.521	1.00	46.00	A	C
ATOM	2469	O	SER	A	571	1.345	9.295	6.762	1.00	46.79	A	O
ATOM	2470	N	ARG	A	572	3.012	10.481	5.800	1.00	46.90	A	N
ATOM	2472	CA	ARG	A	572	2.146	11.585	5.348	1.00	47.52	A	C
ATOM	2474	CB	ARG	A	572	2.414	12.856	6.181	1.00	47.67	A	C
ATOM	2477	CG	ARG	A	572	3.899	13.255	6.343	1.00	48.36	A	C
ATOM	2480	CD	ARG	A	572	4.392	14.299	5.342	1.00	48.94	A	C
ATOM	2483	NE	ARG	A	572	5.846	14.476	5.371	1.00	49.60	A	N
ATOM	2485	CZ	ARG	A	572	6.548	15.158	4.461	1.00	49.93	A	C
ATOM	2486	NH1	ARG	A	572	5.942	15.748	3.432	1.00	49.93	A	N
ATOM	2489	NH2	ARG	A	572	7.869	15.255	4.580	1.00	50.04	A	N
ATOM	2492	C	ARG	A	572	2.299	11.870	3.842	1.00	47.78	A	C
ATOM	2493	O	ARG	A	572	2.330	13.032	3.413	1.00	47.93	A	O
ATOM	2494	N	TYR	A	573	2.348	10.800	3.047	1.00	47.99	A	N
ATOM	2496	CA	TYR	A	573	2.606	10.890	1.604	1.00	48.13	A	C
ATOM	2498	CB	TYR	A	573	3.839	10.038	1.264	1.00	48.32	A	C
ATOM	2501	CG	TYR	A	573	5.090	10.843	0.971	1.00	49.01	A	C
ATOM	2502	CD1	TYR	A	573	5.840	11.408	2.003	1.00	49.66	A	C
ATOM	2504	CE1	TYR	A	573	6.988	12.154	1.736	1.00	50.12	A	C
ATOM	2506	CZ	TYR	A	573	7.396	12.335	0.421	1.00	50.65	A	C
ATOM	2507	OH	TYR	A	573	8.530	13.070	0.141	1.00	51.55	A	O
ATOM	2509	CE2	TYR	A	573	6.668	11.784	-0.618	1.00	50.16	A	C
ATOM	2511	CD2	TYR	A	573	5.522	11.041	-0.340	1.00	49.75	A	C
ATOM	2513	C	TYR	A	573	1.396	10.437	0.749	1.00	47.99	A	C
ATOM	2514	O	TYR	A	573	0.637	9.549	1.157	1.00	48.18	A	O
ATOM	2515	N	ILE	A	574	1.218	11.060	-0.423	1.00	47.68	A	N
ATOM	2517	CA	ILE	A	574	0.221	10.611	-1.414	1.00	47.28	A	C
ATOM	2519	CB	ILE	A	574	-0.335	11.823	-2.263	1.00	47.36	A	C
ATOM	2521	CG1	ILE	A	574	-1.852	11.681	-2.521	1.00	47.24	A	C
ATOM	2524	CD1	ILE	A	574	-2.265	10.667	-3.589	1.00	47.19	A	C
ATOM	2528	CG2	ILE	A	574	0.468	12.038	-3.572	1.00	47.44	A	C
ATOM	2532	C	ILE	A	574	0.819	9.524	-2.312	1.00	46.58	A	C
ATOM	2533	O	ILE	A	574	0.097	8.640	-2.793	1.00	47.04	A	O
ATOM	2534	N	GLU	A	575	2.133	9.598	-2.539	1.00	45.52	A	N
ATOM	2536	CA	GLU	A	575	2.848	8.569	-3.297	1.00	44.42	A	C
ATOM	2538	CB	GLU	A	575	4.131	9.120	-3.949	1.00	44.66	A	C
ATOM	2541	CG	GLU	A	575	4.611	8.287	-5.139	1.00	45.56	A	C
ATOM	2544	CD	GLU	A	575	5.484	9.057	-6.128	1.00	47.20	A	C
ATOM	2545	OE1	GLU	A	575	6.216	9.984	-5.710	1.00	47.38	A	O
ATOM	2546	OE2	GLU	A	575	5.450	8.721	-7.335	1.00	47.58	A	O
ATOM	2547	C	GLU	A	575	3.162	7.383	-2.392	1.00	42.62	A	C
ATOM	2548	O	GLU	A	575	2.802	6.252	-2.726	1.00	43.25	A	O
ATOM	2549	N	ASP	A	576	3.840	7.644	-1.266	1.00	40.22	A	N
ATOM	2551	CA	ASP	A	576	4.075	6.649	-0.202	1.00	37.98	A	C
ATOM	2553	CB	ASP	A	576	2.750	5.995	0.225	1.00	38.18	A	C
ATOM	2556	CG	ASP	A	576	2.910	5.016	1.364	1.00	39.08	A	C
ATOM	2557	OD1	ASP	A	576	2.937	3.796	1.076	1.00	38.78	A	O
ATOM	2558	OD2	ASP	A	576	2.985	5.364	2.570	1.00	41.48	A	O
ATOM	2559	C	ASP	A	576	5.106	5.614	-0.658	1.00	35.29	A	C
ATOM	2560	O	ASP	A	576	5.117	5.222	-1.818	1.00	35.14	A	O
ATOM	2561	N	GLU	A	577	5.977	5.182	0.251	1.00	32.19	A	N
ATOM	2563	CA	GLU	A	577	7.146	4.377	-0.133	1.00	29.90	A	C
ATOM	2565	CB	GLU	A	577	8.307	4.597	0.858	1.00	29.98	A	C
ATOM	2568	CG	GLU	A	577	8.924	5.992	0.745	1.00	29.86	A	C
ATOM	2571	CD	GLU	A	577	10.252	6.149	1.479	1.00	30.30	A	C
ATOM	2572	OE1	GLU	A	577	11.230	5.443	1.141	1.00	27.60	A	O
ATOM	2573	OE2	GLU	A	577	10.322	7.008	2.384	1.00	30.64	A	O
ATOM	2574	C	GLU	A	577	6.838	2.878	-0.335	1.00	27.95	A	C
ATOM	2575	O	GLU	A	577	7.741	2.092	-0.617	1.00	26.38	A	O
ATOM	2576	N	ASP	A	578	5.568	2.488	-0.214	1.00	25.79	A	N
ATOM	2578	CA	ASP	A	578	5.152	1.130	-0.565	1.00	24.73	A	C
ATOM	2580	CB	ASP	A	578	3.756	0.802	-0.009	1.00	24.59	A	C

ATOM	2583	CG	ASP	A	578	3.755	0.507	1.479	1.00	24.22	A	C
ATOM	2584	OD1	ASP	A	578	4.758	0.759	2.173	1.00	22.79	A	O
ATOM	2585	OD2	ASP	A	578	2.761	0.021	2.040	1.00	23.67	A	O
ATOM	2586	C	ASP	A	578	5.113	0.914	-2.085	1.00	24.30	A	C
ATOM	2587	O	ASP	A	578	5.010	-0.223	-2.538	1.00	22.85	A	O
ATOM	2588	N	TYR	A	579	5.172	2.001	-2.859	1.00	24.45	A	N
ATOM	2590	CA	TYR	A	579	5.029	1.934	-4.315	1.00	25.01	A	C
ATOM	2592	CB	TYR	A	579	3.928	2.908	-4.770	1.00	25.04	A	C
ATOM	2595	CG	TYR	A	579	2.556	2.582	-4.218	1.00	24.47	A	C
ATOM	2596	CD1	TYR	A	579	2.195	2.963	-2.928	1.00	25.69	A	C
ATOM	2598	CE1	TYR	A	579	0.932	2.665	-2.409	1.00	25.75	A	C
ATOM	2600	CZ	TYR	A	579	0.022	1.977	-3.187	1.00	25.29	A	C
ATOM	2601	OH	TYR	A	579	-1.217	1.675	-2.675	1.00	25.28	A	O
ATOM	2603	CE2	TYR	A	579	0.358	1.577	-4.475	1.00	25.54	A	C
ATOM	2605	CD2	TYR	A	579	1.620	1.886	-4.984	1.00	26.01	A	C
ATOM	2607	C	TYR	A	579	6.329	2.209	-5.093	1.00	25.81	A	C
ATOM	2608	O	TYR	A	579	6.401	1.925	-6.285	1.00	26.17	A	O
ATOM	2609	N	TYR	A	580	7.349	2.751	-4.435	1.00	26.41	A	N
ATOM	2611	CA	TYR	A	580	8.617	3.046	-5.106	1.00	26.93	A	C
ATOM	2613	CB	TYR	A	580	8.598	4.475	-5.677	1.00	27.09	A	C
ATOM	2616	CG	TYR	A	580	8.584	5.554	-4.622	1.00	26.95	A	C
ATOM	2617	CD1	TYR	A	580	9.771	6.087	-4.123	1.00	27.01	A	C
ATOM	2619	CE1	TYR	A	580	9.764	7.069	-3.135	1.00	27.38	A	C
ATOM	2621	CZ	TYR	A	580	8.558	7.541	-2.647	1.00	28.47	A	C
ATOM	2622	OH	TYR	A	580	8.545	8.516	-1.674	1.00	29.60	A	O
ATOM	2624	CE2	TYR	A	580	7.363	7.032	-3.132	1.00	28.07	A	C
ATOM	2626	CD2	TYR	A	580	7.381	6.043	-4.113	1.00	27.45	A	C
ATOM	2628	C	TYR	A	580	9.823	2.867	-4.183	1.00	27.08	A	C
ATOM	2629	O	TYR	A	580	9.705	2.962	-2.949	1.00	27.01	A	O
ATOM	2630	N	LYS	A	581	10.981	2.607	-4.787	1.00	27.09	A	N
ATOM	2632	CA	LYS	A	581	12.230	2.554	-4.044	1.00	27.49	A	C
ATOM	2634	CB	LYS	A	581	13.167	1.469	-4.591	1.00	27.82	A	C
ATOM	2637	CG	LYS	A	581	12.624	0.066	-4.493	1.00	29.08	A	C
ATOM	2640	CD	LYS	A	581	12.553	-0.410	-3.054	1.00	29.95	A	C
ATOM	2643	CE	LYS	A	581	12.586	-1.923	-2.981	1.00	30.16	A	C
ATOM	2646	NZ	LYS	A	581	13.933	-2.487	-3.300	1.00	31.13	A	N
ATOM	2650	C	LYS	A	581	12.913	3.910	-4.147	1.00	27.35	A	C
ATOM	2651	O	LYS	A	581	13.313	4.327	-5.244	1.00	27.59	A	O
ATOM	2652	N	ALA	A	582	13.045	4.587	-3.008	1.00	26.87	A	N
ATOM	2654	CA	ALA	A	582	13.721	5.877	-2.940	1.00	27.05	A	C
ATOM	2656	CB	ALA	A	582	13.460	6.524	-1.587	1.00	27.03	A	C
ATOM	2660	C	ALA	A	582	15.219	5.686	-3.147	1.00	27.17	A	C
ATOM	2661	O	ALA	A	582	15.770	4.669	-2.733	1.00	26.90	A	O
ATOM	2662	N	SER	A	583	15.875	6.657	-3.789	1.00	26.98	A	N
ATOM	2664	CA	SER	A	583	17.342	6.691	-3.818	1.00	27.27	A	C
ATOM	2666	CB	SER	A	583	17.864	7.934	-4.568	1.00	27.02	A	C
ATOM	2669	OG	SER	A	583	17.666	7.842	-5.971	1.00	24.95	A	O
ATOM	2671	C	SER	A	583	17.899	6.673	-2.390	1.00	27.51	A	C
ATOM	2672	O	SER	A	583	18.853	5.960	-2.111	1.00	28.19	A	O
ATOM	2673	N	VAL	A	584	17.301	7.481	-1.511	1.00	27.95	A	N
ATOM	2675	CA	VAL	A	584	17.624	7.547	-0.081	1.00	27.95	A	C
ATOM	2677	CB	VAL	A	584	18.359	8.860	0.279	1.00	28.18	A	C
ATOM	2679	CG1	VAL	A	584	18.684	8.910	1.762	1.00	29.19	A	C
ATOM	2683	CG2	VAL	A	584	19.610	8.997	-0.529	1.00	28.53	A	C
ATOM	2687	C	VAL	A	584	16.314	7.499	0.716	1.00	27.93	A	C
ATOM	2688	O	VAL	A	584	15.532	8.445	0.693	1.00	27.03	A	O
ATOM	2689	N	THR	A	585	16.072	6.403	1.428	1.00	28.20	A	N
ATOM	2691	CA	THR	A	585	14.795	6.239	2.111	1.00	28.72	A	C
ATOM	2693	CB	THR	A	585	14.394	4.744	2.181	1.00	28.79	A	C
ATOM	2695	OG1	THR	A	585	13.033	4.623	2.621	1.00	29.29	A	O
ATOM	2697	CG2	THR	A	585	15.193	3.992	3.216	1.00	29.13	A	C
ATOM	2701	C	THR	A	585	14.779	6.882	3.494	1.00	28.58	A	C
ATOM	2702	O	THR	A	585	15.809	7.081	4.129	1.00	29.24	A	O
ATOM	2703	N	ARG	A	586	13.572	7.185	3.951	1.00	28.53	A	N
ATOM	2705	CA	ARG	A	586	13.331	7.764	5.266	1.00	27.88	A	C
ATOM	2707	CB	ARG	A	586	12.163	8.751	5.159	1.00	28.97	A	C
ATOM	2710	CG	ARG	A	586	12.163	9.613	3.892	1.00	32.87	A	C

ATOM	2713	CD	ARG	A	586	11.091	10.706	3.880	1.00	37.35	A	C
ATOM	2716	NE	ARG	A	586	11.446	11.869	4.700	1.00	40.84	A	N
ATOM	2718	CZ	ARG	A	586	12.287	12.850	4.340	1.00	42.20	A	C
ATOM	2719	NH1	ARG	A	586	12.897	12.839	3.157	1.00	42.91	A	N
ATOM	2722	NH2	ARG	A	586	12.524	13.854	5.183	1.00	42.67	A	N
ATOM	2725	C	ARG	A	586	12.978	6.639	6.271	1.00	25.82	A	C
ATOM	2726	O	ARG	A	586	12.956	6.850	7.485	1.00	25.52	A	O
ATOM	2727	N	LEU	A	587	12.724	5.449	5.742	1.00	23.19	A	N
ATOM	2729	CA	LEU	A	587	12.216	4.320	6.520	1.00	21.02	A	C
ATOM	2731	CB	LEU	A	587	11.740	3.228	5.569	1.00	21.26	A	C
ATOM	2734	CG	LEU	A	587	10.591	3.508	4.618	1.00	22.52	A	C
ATOM	2736	CD1	LEU	A	587	10.428	2.299	3.713	1.00	23.24	A	C
ATOM	2740	CD2	LEU	A	587	9.314	3.812	5.391	1.00	23.89	A	C
ATOM	2744	C	LEU	A	587	13.303	3.726	7.410	1.00	19.25	A	C
ATOM	2745	O	LEU	A	587	14.475	3.822	7.075	1.00	18.79	A	O
ATOM	2746	N	PRO	A	588	12.911	3.068	8.506	1.00	16.35	A	N
ATOM	2747	CA	PRO	A	588	13.877	2.494	9.451	1.00	14.93	A	C
ATOM	2749	CB	PRO	A	588	13.037	2.286	10.717	1.00	14.98	A	C
ATOM	2752	CG	PRO	A	588	11.683	1.973	10.177	1.00	15.18	A	C
ATOM	2755	CD	PRO	A	588	11.513	2.828	8.927	1.00	16.26	A	C
ATOM	2758	C	PRO	A	588	14.465	1.175	8.947	1.00	13.29	A	C
ATOM	2759	O	PRO	A	588	14.183	0.083	9.484	1.00	12.58	A	O
ATOM	2760	N	ILE	A	589	15.309	1.281	7.925	1.00	11.92	A	N
ATOM	2762	CA	ILE	A	589	15.866	0.118	7.230	1.00	11.54	A	C
ATOM	2764	CB	ILE	A	589	16.889	0.600	6.152	1.00	11.43	A	C
ATOM	2766	CG1	ILE	A	589	16.174	1.366	5.024	1.00	13.60	A	C
ATOM	2769	CD1	ILE	A	589	15.092	0.544	4.305	1.00	14.47	A	C
ATOM	2773	CG2	ILE	A	589	17.700	-0.581	5.601	1.00	12.99	A	C
ATOM	2777	C	ILE	A	589	16.574	-0.864	8.203	1.00	10.07	A	C
ATOM	2778	O	ILE	A	589	16.471	-2.075	8.055	1.00	9.44	A	O
ATOM	2779	N	LYS	A	590	17.300	-0.330	9.186	1.00	9.76	A	N
ATOM	2781	CA	LYS	A	590	18.065	-1.186	10.109	1.00	9.66	A	C
ATOM	2783	CB	LYS	A	590	19.111	-0.377	10.888	1.00	9.94	A	C
ATOM	2786	CG	LYS	A	590	20.252	0.122	10.016	1.00	10.30	A	C
ATOM	2789	CD	LYS	A	590	21.098	1.207	10.703	1.00	10.44	A	C
ATOM	2792	CE	LYS	A	590	22.248	1.579	9.797	1.00	12.41	A	C
ATOM	2795	NZ	LYS	A	590	23.160	2.618	10.380	1.00	12.07	A	N
ATOM	2799	C	LYS	A	590	17.174	-1.954	11.068	1.00	9.73	A	C
ATOM	2800	O	LYS	A	590	17.660	-2.830	11.790	1.00	9.50	A	O
ATOM	2801	N	TRP	A	591	15.876	-1.628	11.089	1.00	9.17	A	N
ATOM	2803	CA	TRP	A	591	14.905	-2.339	11.912	1.00	9.87	A	C
ATOM	2805	CB	TRP	A	591	14.017	-1.349	12.662	1.00	9.98	A	C
ATOM	2808	CG	TRP	A	591	14.655	-0.542	13.766	1.00	11.71	A	C
ATOM	2809	CD1	TRP	A	591	14.457	-0.709	15.103	1.00	12.20	A	C
ATOM	2811	NE1	TRP	A	591	15.141	0.252	15.803	1.00	13.37	A	N
ATOM	2813	CE2	TRP	A	591	15.793	1.065	14.924	1.00	12.15	A	C
ATOM	2814	CD2	TRP	A	591	15.490	0.607	13.627	1.00	13.10	A	C
ATOM	2815	CE3	TRP	A	591	16.031	1.299	12.533	1.00	12.17	A	C
ATOM	2817	CZ3	TRP	A	591	16.853	2.386	12.772	1.00	15.31	A	C
ATOM	2819	CH2	TRP	A	591	17.127	2.813	14.082	1.00	13.32	A	C
ATOM	2821	CZ2	TRP	A	591	16.621	2.156	15.161	1.00	12.48	A	C
ATOM	2823	C	TRP	A	591	13.997	-3.282	11.108	1.00	9.92	A	C
ATOM	2824	O	TRP	A	591	13.223	-4.039	11.706	1.00	10.09	A	O
ATOM	2825	N	MET	A	592	14.096	-3.251	9.773	1.00	9.75	A	N
ATOM	2827	CA	MET	A	592	13.094	-3.843	8.881	1.00	9.99	A	C
ATOM	2829	CB	MET	A	592	12.876	-2.908	7.667	1.00	9.83	A	C
ATOM	2832	CG	MET	A	592	12.051	-1.676	7.999	1.00	11.13	A	C
ATOM	2835	SD	MET	A	592	12.111	-0.339	6.763	1.00	14.42	A	S
ATOM	2836	CE	MET	A	592	11.786	-1.271	5.270	1.00	11.86	A	C
ATOM	2840	C	MET	A	592	13.432	-5.244	8.373	1.00	9.53	A	C
ATOM	2841	O	MET	A	592	14.602	-5.589	8.192	1.00	10.45	A	O
ATOM	2842	N	SER	A	593	12.395	-6.034	8.118	1.00	9.01	A	N
ATOM	2844	CA	SER	A	593	12.558	-7.391	7.605	1.00	9.63	A	C
ATOM	2846	CB	SER	A	593	11.241	-8.149	7.607	1.00	10.07	A	C
ATOM	2849	OG	SER	A	593	10.406	-7.605	6.617	1.00	10.36	A	O
ATOM	2851	C	SER	A	593	13.073	-7.313	6.164	1.00	9.56	A	C
ATOM	2852	O	SER	A	593	12.921	-6.287	5.511	1.00	10.05	A	O

ATOM	2853	N	PRO	A	594	13.695	-8.378	5.686	1.00	10.88	A	N
ATOM	2854	CA	PRO	A	594	14.197	-8.420	4.301	1.00	11.51	A	C
ATOM	2856	CB	PRO	A	594	14.787	-9.828	4.191	1.00	12.13	A	C
ATOM	2859	CG	PRO	A	594	15.141	-10.176	5.577	1.00	12.75	A	C
ATOM	2862	CD	PRO	A	594	14.022	-9.610	6.420	1.00	10.32	A	C
ATOM	2865	C	PRO	A	594	13.108	-8.199	3.254	1.00	11.67	A	C
ATOM	2866	O	PRO	A	594	13.366	-7.517	2.289	1.00	12.87	A	O
ATOM	2867	N	GLU	A	595	11.916	-8.754	3.455	1.00	12.18	A	N
ATOM	2869	CA	GLU	A	595	10.819	-8.588	2.509	1.00	11.54	A	C
ATOM	2871	CB	GLU	A	595	9.685	-9.578	2.796	1.00	11.95	A	C
ATOM	2874	CG	GLU	A	595	8.905	-9.349	4.080	1.00	12.54	A	C
ATOM	2877	CD	GLU	A	595	9.410	-10.169	5.261	1.00	12.35	A	C
ATOM	2878	OE1	GLU	A	595	10.587	-10.628	5.259	1.00	12.67	A	O
ATOM	2879	OE2	GLU	A	595	8.624	-10.313	6.232	1.00	11.80	A	O
ATOM	2880	C	GLU	A	595	10.325	-7.139	2.494	1.00	11.35	A	C
ATOM	2881	O	GLU	A	595	9.870	-6.621	1.462	1.00	10.36	A	O
ATOM	2882	N	SER	A	596	10.453	-6.468	3.639	1.00	11.09	A	N
ATOM	2884	CA	SER	A	596	10.129	-5.054	3.746	1.00	11.11	A	C
ATOM	2886	CB	SER	A	596	10.035	-4.639	5.215	1.00	11.61	A	C
ATOM	2889	OG	SER	A	596	9.071	-5.412	5.916	1.00	10.96	A	O
ATOM	2891	C	SER	A	596	11.154	-4.165	3.009	1.00	11.46	A	C
ATOM	2892	O	SER	A	596	10.780	-3.187	2.349	1.00	11.08	A	O
ATOM	2893	N	ILE	A	597	12.433	-4.494	3.154	1.00	11.82	A	N
ATOM	2895	CA	ILE	A	597	13.498	-3.793	2.447	1.00	12.20	A	C
ATOM	2897	CB	ILE	A	597	14.870	-4.196	3.012	1.00	12.29	A	C
ATOM	2899	CG1	ILE	A	597	15.044	-3.734	4.479	1.00	11.10	A	C
ATOM	2902	CD1	ILE	A	597	16.321	-4.267	5.140	1.00	10.75	A	C
ATOM	2906	CG2	ILE	A	597	15.980	-3.586	2.160	1.00	13.21	A	C
ATOM	2910	C	ILE	A	597	13.433	-4.051	0.923	1.00	12.61	A	C
ATOM	2911	O	ILE	A	597	13.521	-3.120	0.135	1.00	14.25	A	O
ATOM	2912	N	ASN	A	598	13.275	-5.298	0.514	1.00	12.98	A	N
ATOM	2914	CA	ASN	A	598	13.331	-5.672	-0.919	1.00	14.27	A	C
ATOM	2916	CB	ASN	A	598	13.618	-7.179	-1.052	1.00	14.04	A	C
ATOM	2919	CG	ASN	A	598	15.068	-7.523	-0.790	1.00	16.01	A	C
ATOM	2920	OD1	ASN	A	598	15.971	-6.727	-1.066	1.00	18.13	A	O
ATOM	2921	ND2	ASN	A	598	15.307	-8.734	-0.283	1.00	16.92	A	N
ATOM	2924	C	ASN	A	598	12.077	-5.337	-1.725	1.00	15.32	A	C
ATOM	2925	O	ASN	A	598	12.162	-4.886	-2.877	1.00	15.17	A	O
ATOM	2926	N	PHE	A	599	10.912	-5.552	-1.119	1.00	15.42	A	N
ATOM	2928	CA	PHE	A	599	9.636	-5.496	-1.839	1.00	15.79	A	C
ATOM	2930	CB	PHE	A	599	9.088	-6.914	-2.039	1.00	15.78	A	C
ATOM	2933	CG	PHE	A	599	10.095	-7.884	-2.566	1.00	18.17	A	C
ATOM	2934	CD1	PHE	A	599	10.746	-7.643	-3.769	1.00	20.18	A	C
ATOM	2936	CE1	PHE	A	599	11.694	-8.537	-4.245	1.00	21.90	A	C
ATOM	2938	CZ	PHE	A	599	11.975	-9.693	-3.532	1.00	20.74	A	C
ATOM	2940	CE2	PHE	A	599	11.318	-9.945	-2.336	1.00	21.69	A	C
ATOM	2942	CD2	PHE	A	599	10.391	-9.038	-1.860	1.00	19.49	A	C
ATOM	2944	C	PHE	A	599	8.574	-4.641	-1.156	1.00	15.14	A	C
ATOM	2945	O	PHE	A	599	7.427	-4.610	-1.608	1.00	15.42	A	O
ATOM	2946	N	ARG	A	600	8.951	-3.936	-0.092	1.00	15.13	A	N
ATOM	2948	CA	ARG	A	600	8.024	-3.137	0.701	1.00	15.85	A	C
ATOM	2950	CB	ARG	A	600	7.614	-1.880	-0.076	1.00	16.31	A	C
ATOM	2953	CG	ARG	A	600	8.784	-0.950	-0.377	1.00	17.77	A	C
ATOM	2956	CD	ARG	A	600	9.269	-0.173	0.835	1.00	18.17	A	C
ATOM	2959	NE	ARG	A	600	10.355	0.750	0.508	1.00	20.72	A	N
ATOM	2961	CZ	ARG	A	600	11.657	0.490	0.633	1.00	21.90	A	C
ATOM	2962	NH1	ARG	A	600	12.094	-0.680	1.078	1.00	22.93	A	N
ATOM	2965	NH2	ARG	A	600	12.543	1.419	0.299	1.00	22.61	A	N
ATOM	2968	C	ARG	A	600	6.793	-3.956	1.149	1.00	15.58	A	C
ATOM	2969	O	ARG	A	600	5.653	-3.464	1.136	1.00	15.40	A	O
ATOM	2970	N	ARG	A	601	7.046	-5.206	1.535	1.00	15.64	A	N
ATOM	2972	CA	ARG	A	601	6.022	-6.120	2.052	1.00	16.29	A	C
ATOM	2974	CB	ARG	A	601	6.363	-7.569	1.724	1.00	17.23	A	C
ATOM	2977	CG	ARG	A	601	6.233	-7.938	0.259	1.00	21.68	A	C
ATOM	2980	CD	ARG	A	601	5.955	-9.440	-0.022	1.00	25.56	A	C
ATOM	2983	NE	ARG	A	601	6.621	-9.837	-1.270	1.00	30.36	A	N
ATOM	2985	CZ	ARG	A	601	6.043	-10.295	-2.379	1.00	31.71	A	C

ATOM	2986	NH1	ARG	A	601	4.738	-10.497	-2.462	1.00	34.89	A	N
ATOM	2989	NH2	ARG	A	601	6.800	-10.599	-3.428	1.00	34.61	A	N
ATOM	2992	C	ARG	A	601	6.002	-5.963	3.571	1.00	15.73	A	C
ATOM	2993	O	ARG	A	601	7.033	-6.218	4.233	1.00	15.42	A	O
ATOM	2994	N	PHE	A	602	4.866	-5.511	4.105	1.00	14.28	A	N
ATOM	2996	CA	PHE	A	602	4.684	-5.323	5.543	1.00	14.03	A	C
ATOM	2998	CB	PHE	A	602	4.463	-3.844	5.876	1.00	13.94	A	C
ATOM	3001	CG	PHE	A	602	5.599	-2.947	5.501	1.00	15.36	A	C
ATOM	3002	CD1	PHE	A	602	6.596	-2.632	6.430	1.00	16.03	A	C
ATOM	3004	CE1	PHE	A	602	7.651	-1.772	6.090	1.00	15.79	A	C
ATOM	3006	CZ	PHE	A	602	7.690	-1.198	4.833	1.00	15.40	A	C
ATOM	3008	CE2	PHE	A	602	6.686	-1.485	3.909	1.00	15.83	A	C
ATOM	3010	CD2	PHE	A	602	5.643	-2.348	4.245	1.00	14.53	A	C
ATOM	3012	C	PHE	A	602	3.499	-6.130	6.054	1.00	13.39	A	C
ATOM	3013	O	PHE	A	602	2.353	-5.927	5.631	1.00	13.20	A	O
ATOM	3014	N	THR	A	603	3.766	-7.070	6.947	1.00	13.12	A	N
ATOM	3016	CA	THR	A	603	2.739	-7.941	7.518	1.00	12.82	A	C
ATOM	3018	CB	THR	A	603	2.851	-9.331	6.902	1.00	13.20	A	C
ATOM	3020	OG1	THR	A	603	4.143	-9.881	7.212	1.00	13.90	A	O
ATOM	3022	CG2	THR	A	603	2.771	-9.277	5.357	1.00	14.67	A	C
ATOM	3026	C	THR	A	603	2.968	-8.095	9.007	1.00	12.15	A	C
ATOM	3027	O	THR	A	603	3.936	-7.588	9.552	1.00	10.36	A	O
ATOM	3028	N	THR	A	604	2.125	-8.874	9.659	1.00	11.47	A	N
ATOM	3030	CA	THR	A	604	2.387	-9.169	11.053	1.00	11.50	A	C
ATOM	3032	CB	THR	A	604	1.228	-9.955	11.676	1.00	12.26	A	C
ATOM	3034	OG1	THR	A	604	0.043	-9.138	11.648	1.00	14.28	A	O
ATOM	3036	CG2	THR	A	604	1.493	-10.182	13.155	1.00	14.14	A	C
ATOM	3040	C	THR	A	604	3.728	-9.884	11.203	1.00	11.13	A	C
ATOM	3041	O	THR	A	604	4.391	-9.699	12.211	1.00	9.85	A	O
ATOM	3042	N	ALA	A	605	4.142	-10.679	10.206	1.00	10.23	A	N
ATOM	3044	CA	ALA	A	605	5.450	-11.338	10.258	1.00	10.32	A	C
ATOM	3046	CB	ALA	A	605	5.608	-12.374	9.156	1.00	10.78	A	C
ATOM	3050	C	ALA	A	605	6.611	-10.363	10.197	1.00	9.56	A	C
ATOM	3051	O	ALA	A	605	7.640	-10.616	10.824	1.00	8.50	A	O
ATOM	3052	N	SER	A	606	6.459	-9.272	9.445	1.00	8.64	A	N
ATOM	3054	CA	SER	A	606	7.486	-8.245	9.412	1.00	9.24	A	C
ATOM	3056	CB	SER	A	606	7.352	-7.296	8.190	1.00	9.76	A	C
ATOM	3059	OG	SER	A	606	6.179	-6.496	8.250	1.00	10.66	A	O
ATOM	3061	C	SER	A	606	7.505	-7.489	10.748	1.00	9.16	A	C
ATOM	3062	O	SER	A	606	8.572	-7.100	11.211	1.00	8.11	A	O
ATOM	3063	N	ASP	A	607	6.340	-7.307	11.379	1.00	8.37	A	N
ATOM	3065	CA	ASP	A	607	6.297	-6.717	12.720	1.00	8.68	A	C
ATOM	3067	CB	ASP	A	607	4.876	-6.507	13.225	1.00	8.94	A	C
ATOM	3070	CG	ASP	A	607	4.256	-5.197	12.785	1.00	11.42	A	C
ATOM	3071	OD1	ASP	A	607	4.925	-4.280	12.218	1.00	11.99	A	O
ATOM	3072	OD2	ASP	A	607	3.029	-5.001	13.022	1.00	12.74	A	O
ATOM	3073	C	ASP	A	607	7.034	-7.616	13.740	1.00	8.12	A	C
ATOM	3074	O	ASP	A	607	7.628	-7.111	14.678	1.00	7.11	A	O
ATOM	3075	N	VAL	A	608	6.952	-8.940	13.577	1.00	7.25	A	N
ATOM	3077	CA	VAL	A	608	7.677	-9.870	14.461	1.00	7.14	A	C
ATOM	3079	CB	VAL	A	608	7.280	-11.342	14.171	1.00	6.69	A	C
ATOM	3081	CG1	VAL	A	608	8.277	-12.331	14.822	1.00	8.13	A	C
ATOM	3085	CG2	VAL	A	608	5.840	-11.616	14.668	1.00	7.95	A	C
ATOM	3089	C	VAL	A	608	9.187	-9.687	14.332	1.00	7.61	A	C
ATOM	3090	O	VAL	A	608	9.902	-9.615	15.345	1.00	6.65	A	O
ATOM	3091	N	TRP	A	609	9.673	-9.587	13.090	1.00	7.07	A	N
ATOM	3093	CA	TRP	A	609	11.085	-9.274	12.835	1.00	7.28	A	C
ATOM	3095	CB	TRP	A	609	11.349	-9.095	11.329	1.00	7.08	A	C
ATOM	3098	CG	TRP	A	609	12.771	-8.707	10.985	1.00	7.95	A	C
ATOM	3099	CD1	TRP	A	609	13.381	-7.506	11.228	1.00	7.59	A	C
ATOM	3101	NE1	TRP	A	609	14.692	-7.555	10.821	1.00	8.83	A	N
ATOM	3103	CE2	TRP	A	609	14.958	-8.799	10.310	1.00	8.13	A	C
ATOM	3104	CD2	TRP	A	609	13.778	-9.555	10.414	1.00	6.30	A	C
ATOM	3105	CE3	TRP	A	609	13.779	-10.881	9.934	1.00	6.84	A	C
ATOM	3107	CZ3	TRP	A	609	14.944	-11.401	9.398	1.00	8.38	A	C
ATOM	3109	CH2	TRP	A	609	16.108	-10.624	9.313	1.00	7.22	A	C
ATOM	3111	CZ2	TRP	A	609	16.135	-9.313	9.749	1.00	8.92	A	C

ATOM	3113	C	TRP	A	609	11.484	-7.994	13.602	1.00	7.00	A	C
ATOM	3114	O	TRP	A	609	12.484	-7.969	14.329	1.00	7.89	A	O
ATOM	3115	N	MET	A	610	10.687	-6.954	13.449	1.00	7.31	A	N
ATOM	3117	CA	MET	A	610	11.019	-5.634	13.979	1.00	7.12	A	C
ATOM	3119	CB	MET	A	610	10.083	-4.569	13.380	1.00	7.25	A	C
ATOM	3122	CG	MET	A	610	10.433	-3.155	13.777	1.00	8.77	A	C
ATOM	3125	SD	MET	A	610	9.336	-1.944	13.037	1.00	11.18	A	S
ATOM	3126	CE	MET	A	610	10.448	-0.489	13.042	1.00	12.69	A	C
ATOM	3130	C	MET	A	610	10.945	-5.628	15.504	1.00	7.16	A	C
ATOM	3131	O	MET	A	610	11.740	-4.979	16.171	1.00	7.31	A	O
ATOM	3132	N	PHE	A	611	9.995	-6.376	16.053	1.00	7.20	A	N
ATOM	3134	CA	PHE	A	611	9.859	-6.506	17.503	1.00	6.98	A	C
ATOM	3136	CB	PHE	A	611	8.614	-7.289	17.857	1.00	7.02	A	C
ATOM	3139	CG	PHE	A	611	8.576	-7.724	19.296	1.00	8.33	A	C
ATOM	3140	CD1	PHE	A	611	8.329	-6.808	20.294	1.00	9.98	A	C
ATOM	3142	CE1	PHE	A	611	8.322	-7.188	21.610	1.00	9.82	A	C
ATOM	3144	CZ	PHE	A	611	8.587	-8.482	21.958	1.00	9.72	A	C
ATOM	3146	CE2	PHE	A	611	8.835	-9.415	20.984	1.00	11.54	A	C
ATOM	3148	CD2	PHE	A	611	8.838	-9.033	19.645	1.00	9.39	A	C
ATOM	3150	C	PHE	A	611	11.103	-7.142	18.153	1.00	6.73	A	C
ATOM	3151	O	PHE	A	611	11.557	-6.708	19.202	1.00	7.59	A	O
ATOM	3152	N	ALA	A	612	11.692	-8.119	17.491	1.00	7.27	A	N
ATOM	3154	CA	ALA	A	612	12.922	-8.703	17.973	1.00	7.36	A	C
ATOM	3156	CB	ALA	A	612	13.212	-9.987	17.272	1.00	7.52	A	C
ATOM	3160	C	ALA	A	612	14.090	-7.718	17.877	1.00	7.40	A	C
ATOM	3161	O	ALA	A	612	14.984	-7.738	18.735	1.00	7.06	A	O
ATOM	3162	N	VAL	A	613	14.094	-6.842	16.868	1.00	7.17	A	N
ATOM	3164	CA	VAL	A	613	15.098	-5.779	16.831	1.00	7.65	A	C
ATOM	3166	CB	VAL	A	613	15.096	-4.939	15.516	1.00	7.18	A	C
ATOM	3168	CG1	VAL	A	613	16.183	-3.867	15.575	1.00	8.13	A	C
ATOM	3172	CG2	VAL	A	613	15.284	-5.822	14.301	1.00	8.64	A	C
ATOM	3176	C	VAL	A	613	14.874	-4.843	18.018	1.00	7.44	A	C
ATOM	3177	O	VAL	A	613	15.816	-4.438	18.663	1.00	7.86	A	O
ATOM	3178	N	CYS	A	614	13.628	-4.521	18.312	1.00	7.31	A	N
ATOM	3180	CA	CYS	A	614	13.304	-3.712	19.482	1.00	7.38	A	C
ATOM	3182	CB	CYS	A	614	11.808	-3.409	19.500	1.00	7.62	A	C
ATOM	3185	SG	CYS	A	614	11.279	-2.363	20.856	1.00	12.24	A	S
ATOM	3186	C	CYS	A	614	13.803	-4.393	20.791	1.00	7.51	A	C
ATOM	3187	O	CYS	A	614	14.404	-3.737	21.652	1.00	8.23	A	O
ATOM	3188	N	MET	A	615	13.602	-5.700	20.939	1.00	6.99	A	N
ATOM	3190	CA	MET	A	615	14.136	-6.415	22.104	1.00	8.46	A	C
ATOM	3192	CB	MET	A	615	13.727	-7.893	22.087	1.00	8.91	A	C
ATOM	3195	CG	MET	A	615	12.273	-8.132	22.309	1.00	11.03	A	C
ATOM	3198	SD	MET	A	615	12.003	-9.900	22.802	1.00	14.28	A	S
ATOM	3199	CE	MET	A	615	12.231	-10.684	21.273	1.00	13.21	A	C
ATOM	3203	C	MET	A	615	15.657	-6.314	22.182	1.00	7.71	A	C
ATOM	3204	O	MET	A	615	16.223	-6.111	23.249	1.00	8.82	A	O
ATOM	3205	N	TRP	A	616	16.324	-6.420	21.042	1.00	7.61	A	N
ATOM	3207	CA	TRP	A	616	17.773	-6.243	20.982	1.00	7.16	A	C
ATOM	3209	CB	TRP	A	616	18.277	-6.483	19.555	1.00	7.70	A	C
ATOM	3212	CG	TRP	A	616	19.759	-6.411	19.431	1.00	6.78	A	C
ATOM	3213	CD1	TRP	A	616	20.623	-7.465	19.493	1.00	7.50	A	C
ATOM	3215	NE1	TRP	A	616	21.916	-7.021	19.337	1.00	8.34	A	N
ATOM	3217	CE2	TRP	A	616	21.913	-5.665	19.176	1.00	8.17	A	C
ATOM	3218	CD2	TRP	A	616	20.559	-5.247	19.199	1.00	5.69	A	C
ATOM	3219	CE3	TRP	A	616	20.285	-3.876	19.074	1.00	8.29	A	C
ATOM	3221	CZ3	TRP	A	616	21.327	-3.003	18.884	1.00	8.52	A	C
ATOM	3223	CH2	TRP	A	616	22.663	-3.460	18.833	1.00	7.88	A	C
ATOM	3225	CZ2	TRP	A	616	22.964	-4.786	18.940	1.00	8.12	A	C
ATOM	3227	C	TRP	A	616	18.171	-4.841	21.476	1.00	7.53	A	C
ATOM	3228	O	TRP	A	616	19.125	-4.732	22.241	1.00	8.03	A	O
ATOM	3229	N	GLU	A	617	17.425	-3.794	21.081	1.00	7.69	A	N
ATOM	3231	CA	GLU	A	617	17.671	-2.434	21.555	1.00	8.18	A	C
ATOM	3233	CB	GLU	A	617	16.718	-1.416	20.918	1.00	8.57	A	C
ATOM	3236	CG	GLU	A	617	16.871	-1.110	19.441	1.00	10.70	A	C
ATOM	3239	CD	GLU	A	617	15.817	-0.100	19.000	1.00	13.08	A	C
ATOM	3240	OE1	GLU	A	617	16.176	0.998	18.510	1.00	13.59	A	O

ATOM	3241	OE2	GLU	A	617	14.620	-0.372	19.205	1.00	14.34	A	O
ATOM	3242	C	GLU	A	617	17.496	-2.334	23.066	1.00	8.12	A	C
ATOM	3243	O	GLU	A	617	18.304	-1.700	23.749	1.00	8.06	A	O
ATOM	3244	N	ILE	A	618	16.453	-2.970	23.593	1.00	8.10	A	N
ATOM	3246	CA	ILE	A	618	16.172	-2.899	25.027	1.00	8.31	A	C
ATOM	3248	CB	ILE	A	618	14.810	-3.549	25.349	1.00	8.09	A	C
ATOM	3250	CG1	ILE	A	618	13.676	-2.696	24.783	1.00	7.50	A	C
ATOM	3253	CD1	ILE	A	618	12.296	-3.333	24.895	1.00	9.45	A	C
ATOM	3257	CG2	ILE	A	618	14.641	-3.746	26.867	1.00	9.02	A	C
ATOM	3261	C	ILE	A	618	17.314	-3.569	25.805	1.00	8.52	A	C
ATOM	3262	O	ILE	A	618	17.884	-2.983	26.731	1.00	9.07	A	O
ATOM	3263	N	LEU	A	619	17.674	-4.780	25.406	1.00	9.16	A	N
ATOM	3265	CA	LEU	A	619	18.752	-5.517	26.063	1.00	9.73	A	C
ATOM	3267	CB	LEU	A	619	18.742	-6.989	25.626	1.00	10.15	A	C
ATOM	3270	CG	LEU	A	619	17.821	-7.924	26.416	1.00	11.23	A	C
ATOM	3272	CD1	LEU	A	619	18.274	-8.131	27.852	1.00	12.73	A	C
ATOM	3276	CD2	LEU	A	619	16.384	-7.464	26.361	1.00	12.78	A	C
ATOM	3280	C	LEU	A	619	20.132	-4.906	25.858	1.00	9.41	A	C
ATOM	3281	O	LEU	A	619	21.071	-5.239	26.600	1.00	11.30	A	O
ATOM	3282	N	SER	A	620	20.249	-3.996	24.890	1.00	9.34	A	N
ATOM	3284	CA	SER	A	620	21.466	-3.226	24.656	1.00	9.57	A	C
ATOM	3286	CB	SER	A	620	21.748	-3.159	23.147	1.00	9.27	A	C
ATOM	3289	OG	SER	A	620	21.720	-4.438	22.539	1.00	9.62	A	O
ATOM	3291	C	SER	A	620	21.412	-1.788	25.217	1.00	10.03	A	C
ATOM	3292	O	SER	A	620	22.253	-0.958	24.870	1.00	10.13	A	O
ATOM	3293	N	PHE	A	621	20.438	-1.495	26.072	1.00	10.21	A	N
ATOM	3295	CA	PHE	A	621	20.281	-0.168	26.658	1.00	10.99	A	C
ATOM	3297	CB	PHE	A	621	21.380	0.092	27.686	1.00	11.57	A	C
ATOM	3300	CG	PHE	A	621	21.417	-0.916	28.786	1.00	11.76	A	C
ATOM	3301	CD1	PHE	A	621	20.585	-0.777	29.903	1.00	14.73	A	C
ATOM	3303	CE1	PHE	A	621	20.616	-1.720	30.939	1.00	13.38	A	C
ATOM	3305	CZ	PHE	A	621	21.455	-2.806	30.845	1.00	15.10	A	C
ATOM	3307	CE2	PHE	A	621	22.282	-2.966	29.728	1.00	15.45	A	C
ATOM	3309	CD2	PHE	A	621	22.257	-2.020	28.708	1.00	14.11	A	C
ATOM	3311	C	PHE	A	621	20.204	0.974	25.633	1.00	11.51	A	C
ATOM	3312	O	PHE	A	621	20.746	2.054	25.840	1.00	11.76	A	O
ATOM	3313	N	GLY	A	622	19.533	0.715	24.513	1.00	12.15	A	N
ATOM	3315	CA	GLY	A	622	19.195	1.755	23.561	1.00	12.52	A	C
ATOM	3318	C	GLY	A	622	20.125	1.958	22.389	1.00	13.31	A	C
ATOM	3319	O	GLY	A	622	19.957	2.916	21.631	1.00	13.27	A	O
ATOM	3320	N	LYS	A	623	21.117	1.086	22.224	1.00	13.94	A	N
ATOM	3322	CA	LYS	A	623	22.003	1.199	21.072	1.00	14.20	A	C
ATOM	3324	CB	LYS	A	623	23.120	0.167	21.156	1.00	15.30	A	C
ATOM	3327	CG	LYS	A	623	24.036	0.374	22.340	1.00	18.22	A	C
ATOM	3330	CD	LYS	A	623	25.359	-0.349	22.137	1.00	23.13	A	C
ATOM	3333	CE	LYS	A	623	25.198	-1.851	22.058	1.00	23.04	A	C
ATOM	3336	NZ	LYS	A	623	26.022	-2.515	23.072	1.00	22.31	A	N
ATOM	3340	C	LYS	A	623	21.223	1.016	19.765	1.00	13.35	A	C
ATOM	3341	O	LYS	A	623	20.175	0.354	19.732	1.00	12.25	A	O
ATOM	3342	N	GLN	A	624	21.720	1.631	18.694	1.00	12.33	A	N
ATOM	3344	CA	GLN	A	624	21.074	1.532	17.390	1.00	11.79	A	C
ATOM	3346	CB	GLN	A	624	21.471	2.693	16.471	1.00	12.79	A	C
ATOM	3349	CG	GLN	A	624	20.803	2.653	15.092	1.00	16.84	A	C
ATOM	3352	CD	GLN	A	624	21.480	3.512	14.033	1.00	20.72	A	C
ATOM	3353	OE1	GLN	A	624	22.510	3.139	13.484	1.00	22.00	A	O
ATOM	3354	NE2	GLN	A	624	20.863	4.642	13.706	1.00	25.56	A	N
ATOM	3357	C	GLN	A	624	21.484	0.218	16.750	1.00	10.43	A	C
ATOM	3358	O	GLN	A	624	22.674	-0.085	16.700	1.00	9.05	A	O
ATOM	3359	N	PRO	A	625	20.527	-0.543	16.226	1.00	9.21	A	N
ATOM	3360	CA	PRO	A	625	20.857	-1.773	15.510	1.00	8.85	A	C
ATOM	3362	CB	PRO	A	625	19.489	-2.336	15.099	1.00	8.81	A	C
ATOM	3365	CG	PRO	A	625	18.589	-1.182	15.135	1.00	8.12	A	C
ATOM	3368	CD	PRO	A	625	19.077	-0.284	16.226	1.00	8.87	A	C
ATOM	3371	C	PRO	A	625	21.690	-1.483	14.260	1.00	9.18	A	C
ATOM	3372	O	PRO	A	625	21.427	-0.517	13.529	1.00	8.70	A	O
ATOM	3373	N	PHE	A	626	22.699	-2.312	14.017	1.00	8.97	A	N
ATOM	3375	CA	PHE	A	626	23.530	-2.167	12.825	1.00	8.80	A	C

ATOM	3377	CB	PHE	A	626	22.755	-2.516	11.552	1.00	9.35	A	C
ATOM	3380	CG	PHE	A	626	22.317	-3.959	11.476	1.00	7.57	A	C
ATOM	3381	CD1	PHE	A	626	23.263	-4.982	11.428	1.00	8.74	A	C
ATOM	3383	CE1	PHE	A	626	22.880	-6.293	11.333	1.00	7.90	A	C
ATOM	3385	CZ	PHE	A	626	21.544	-6.621	11.266	1.00	9.02	A	C
ATOM	3387	CE2	PHE	A	626	20.584	-5.630	11.313	1.00	7.58	A	C
ATOM	3389	CD2	PHE	A	626	20.967	-4.303	11.402	1.00	7.59	A	C
ATOM	3391	C	PHE	A	626	24.153	-0.762	12.737	1.00	9.81	A	C
ATOM	3392	O	PHE	A	626	24.281	-0.193	11.669	1.00	9.56	A	O
ATOM	3393	N	PHE	A	627	24.554	-0.231	13.879	1.00	9.82	A	N
ATOM	3395	CA	PHE	A	627	25.190	1.088	13.917	1.00	11.48	A	C
ATOM	3397	CB	PHE	A	627	25.448	1.543	15.365	1.00	11.15	A	C
ATOM	3400	CG	PHE	A	627	26.395	0.662	16.150	1.00	11.35	A	C
ATOM	3401	CD1	PHE	A	627	27.774	0.810	16.042	1.00	9.33	A	C
ATOM	3403	CE1	PHE	A	627	28.637	0.017	16.772	1.00	10.69	A	C
ATOM	3405	CZ	PHE	A	627	28.131	-0.911	17.652	1.00	12.10	A	C
ATOM	3407	CE2	PHE	A	627	26.746	-1.042	17.787	1.00	10.84	A	C
ATOM	3409	CD2	PHE	A	627	25.905	-0.256	17.051	1.00	9.05	A	C
ATOM	3411	C	PHE	A	627	26.475	1.142	13.092	1.00	12.51	A	C
ATOM	3412	O	PHE	A	627	26.881	2.214	12.636	1.00	14.55	A	O
ATOM	3413	N	TRP	A	628	27.076	-0.021	12.879	1.00	12.47	A	N
ATOM	3415	CA	TRP	A	628	28.355	-0.158	12.189	1.00	13.92	A	C
ATOM	3417	CB	TRP	A	628	29.085	-1.409	12.710	1.00	13.56	A	C
ATOM	3420	CG	TRP	A	628	28.298	-2.730	12.615	1.00	13.24	A	C
ATOM	3421	CD1	TRP	A	628	28.356	-3.647	11.600	1.00	13.12	A	C
ATOM	3423	NE1	TRP	A	628	27.528	-4.710	11.871	1.00	14.92	A	N
ATOM	3425	CE2	TRP	A	628	26.894	-4.493	13.060	1.00	13.87	A	C
ATOM	3426	CD2	TRP	A	628	27.366	-3.256	13.566	1.00	12.08	A	C
ATOM	3427	CE3	TRP	A	628	26.861	-2.807	14.784	1.00	13.25	A	C
ATOM	3429	CZ3	TRP	A	628	25.928	-3.597	15.468	1.00	13.18	A	C
ATOM	3431	CH2	TRP	A	628	25.490	-4.812	14.935	1.00	12.66	A	C
ATOM	3433	CZ2	TRP	A	628	25.966	-5.276	13.739	1.00	12.17	A	C
ATOM	3435	C	TRP	A	628	28.204	-0.203	10.658	1.00	14.82	A	C
ATOM	3436	O	TRP	A	628	29.199	-0.297	9.938	1.00	16.19	A	O
ATOM	3437	N	LEU	A	629	26.963	-0.177	10.171	1.00	14.95	A	N
ATOM	3439	CA	LEU	A	629	26.653	-0.266	8.744	1.00	15.95	A	C
ATOM	3441	CB	LEU	A	629	25.711	-1.447	8.475	1.00	15.63	A	C
ATOM	3444	CG	LEU	A	629	26.128	-2.866	8.839	1.00	15.85	A	C
ATOM	3446	CD1	LEU	A	629	25.034	-3.791	8.377	1.00	17.66	A	C
ATOM	3450	CD2	LEU	A	629	27.437	-3.241	8.191	1.00	17.21	A	C
ATOM	3454	C	LEU	A	629	25.957	0.991	8.249	1.00	16.16	A	C
ATOM	3455	O	LEU	A	629	25.422	1.767	9.042	1.00	17.19	A	O
ATOM	3456	N	GLU	A	630	26.012	1.200	6.933	1.00	17.08	A	N
ATOM	3458	CA	GLU	A	630	25.159	2.176	6.244	1.00	17.66	A	C
ATOM	3460	CB	GLU	A	630	25.859	2.759	4.990	1.00	18.54	A	C
ATOM	3463	CG	GLU	A	630	27.107	3.592	5.285	1.00	22.16	A	C
ATOM	3466	CD	GLU	A	630	27.834	4.104	4.035	1.00	26.66	A	C
ATOM	3467	OE1	GLU	A	630	28.025	3.347	3.054	1.00	30.10	A	O
ATOM	3468	OE2	GLU	A	630	28.254	5.276	4.041	1.00	31.44	A	O
ATOM	3469	C	GLU	A	630	23.877	1.444	5.840	1.00	16.80	A	C
ATOM	3470	O	GLU	A	630	23.899	0.232	5.644	1.00	16.52	A	O
ATOM	3471	N	ASN	A	631	22.777	2.177	5.693	1.00	16.64	A	N
ATOM	3473	CA	ASN	A	631	21.494	1.588	5.288	1.00	16.86	A	C
ATOM	3475	CB	ASN	A	631	20.444	2.692	5.027	1.00	16.92	A	C
ATOM	3478	CG	ASN	A	631	19.758	3.184	6.315	1.00	18.23	A	C
ATOM	3479	OD1	ASN	A	631	19.981	2.645	7.395	1.00	19.71	A	O
ATOM	3480	ND2	ASN	A	631	18.935	4.230	6.196	1.00	18.99	A	N
ATOM	3483	C	ASN	A	631	21.626	0.674	4.067	1.00	16.54	A	C
ATOM	3484	O	ASN	A	631	21.011	-0.395	4.008	1.00	16.91	A	O
ATOM	3485	N	LYS	A	632	22.435	1.094	3.097	1.00	17.10	A	N
ATOM	3487	CA	LYS	A	632	22.531	0.396	1.817	1.00	17.56	A	C
ATOM	3489	CB	LYS	A	632	23.263	1.260	0.770	1.00	17.78	A	C
ATOM	3492	CG	LYS	A	632	24.756	1.461	0.990	1.00	19.40	A	C
ATOM	3495	CD	LYS	A	632	25.297	2.438	-0.081	1.00	23.92	A	C
ATOM	3498	CE	LYS	A	632	26.787	2.688	0.044	1.00	24.81	A	C
ATOM	3501	NZ	LYS	A	632	27.592	1.430	0.014	1.00	27.18	A	N
ATOM	3505	C	LYS	A	632	23.194	-0.965	1.940	1.00	17.38	A	C

ATOM	3506	O	LYS	A	632	23.086	-1.798	1.040	1.00	17.61	A	O
ATOM	3507	N	ASP	A	633	23.863	-1.195	3.064	1.00	17.62	A	N
ATOM	3509	CA	ASP	A	633	24.618	-2.423	3.287	1.00	17.79	A	C
ATOM	3511	CB	ASP	A	633	25.892	-2.111	4.070	1.00	18.50	A	C
ATOM	3514	CG	ASP	A	633	26.869	-1.242	3.289	1.00	22.13	A	C
ATOM	3515	OD1	ASP	A	633	27.019	-1.425	2.062	1.00	25.82	A	O
ATOM	3516	OD2	ASP	A	633	27.534	-0.344	3.843	1.00	29.08	A	O
ATOM	3517	C	ASP	A	633	23.830	-3.477	4.054	1.00	16.35	A	C
ATOM	3518	O	ASP	A	633	24.244	-4.631	4.106	1.00	16.00	A	O
ATOM	3519	N	VAL	A	634	22.698	-3.086	4.639	1.00	14.77	A	N
ATOM	3521	CA	VAL	A	634	21.941	-3.962	5.535	1.00	14.11	A	C
ATOM	3523	CB	VAL	A	634	20.767	-3.188	6.199	1.00	14.20	A	C
ATOM	3525	CG1	VAL	A	634	19.834	-4.110	6.957	1.00	14.96	A	C
ATOM	3529	CG2	VAL	A	634	21.298	-2.120	7.131	1.00	15.06	A	C
ATOM	3533	C	VAL	A	634	21.448	-5.224	4.823	1.00	13.43	A	C
ATOM	3534	O	VAL	A	634	21.685	-6.339	5.289	1.00	12.23	A	O
ATOM	3535	N	ILE	A	635	20.792	-5.063	3.676	1.00	13.66	A	N
ATOM	3537	CA	ILE	A	635	20.175	-6.214	3.010	1.00	13.87	A	C
ATOM	3539	CB	ILE	A	635	19.308	-5.792	1.786	1.00	14.01	A	C
ATOM	3541	CG1	ILE	A	635	18.407	-6.942	1.344	1.00	13.90	A	C
ATOM	3544	CD1	ILE	A	635	17.406	-7.408	2.394	1.00	14.48	A	C
ATOM	3548	CG2	ILE	A	635	20.169	-5.256	0.628	1.00	14.55	A	C
ATOM	3552	C	ILE	A	635	21.205	-7.287	2.666	1.00	14.30	A	C
ATOM	3553	O	ILE	A	635	20.961	-8.467	2.912	1.00	13.32	A	O
ATOM	3554	N	GLY	A	636	22.369	-6.865	2.167	1.00	14.75	A	N
ATOM	3556	CA	GLY	A	636	23.483	-7.771	1.868	1.00	14.87	A	C
ATOM	3559	C	GLY	A	636	23.898	-8.630	3.048	1.00	14.75	A	C
ATOM	3560	O	GLY	A	636	24.068	-9.846	2.937	1.00	14.77	A	O
ATOM	3561	N	VAL	A	637	24.046	-7.989	4.195	1.00	14.62	A	N
ATOM	3563	CA	VAL	A	637	24.396	-8.669	5.431	1.00	14.71	A	C
ATOM	3565	CB	VAL	A	637	24.620	-7.610	6.548	1.00	15.24	A	C
ATOM	3567	CG1	VAL	A	637	24.587	-8.215	7.928	1.00	15.93	A	C
ATOM	3571	CG2	VAL	A	637	25.932	-6.869	6.295	1.00	16.95	A	C
ATOM	3575	C	VAL	A	637	23.336	-9.700	5.841	1.00	14.05	A	C
ATOM	3576	O	VAL	A	637	23.644	-10.829	6.188	1.00	13.96	A	O
ATOM	3577	N	LEU	A	638	22.074	-9.322	5.779	1.00	13.42	A	N
ATOM	3579	CA	LEU	A	638	20.995	-10.231	6.146	1.00	13.52	A	C
ATOM	3581	CB	LEU	A	638	19.669	-9.472	6.179	1.00	13.37	A	C
ATOM	3584	CG	LEU	A	638	19.587	-8.329	7.203	1.00	12.38	A	C
ATOM	3586	CD1	LEU	A	638	18.240	-7.644	7.078	1.00	12.99	A	C
ATOM	3590	CD2	LEU	A	638	19.783	-8.855	8.587	1.00	13.05	A	C
ATOM	3594	C	LEU	A	638	20.902	-11.427	5.188	1.00	14.41	A	C
ATOM	3595	O	LEU	A	638	20.640	-12.547	5.617	1.00	13.64	A	O
ATOM	3596	N	GLU	A	639	21.119	-11.170	3.897	1.00	15.99	A	N
ATOM	3598	CA	GLU	A	639	21.032	-12.204	2.860	1.00	17.38	A	C
ATOM	3600	CB	GLU	A	639	20.974	-11.585	1.446	1.00	17.84	A	C
ATOM	3603	CG	GLU	A	639	19.567	-11.053	1.155	1.00	19.95	A	C
ATOM	3606	CD	GLU	A	639	19.349	-10.385	-0.196	1.00	24.27	A	C
ATOM	3607	OE1	GLU	A	639	20.314	-9.998	-0.890	1.00	26.43	A	O
ATOM	3608	OE2	GLU	A	639	18.156	-10.234	-0.555	1.00	28.41	A	O
ATOM	3609	C	GLU	A	639	22.171	-13.190	3.015	1.00	18.02	A	C
ATOM	3610	O	GLU	A	639	21.998	-14.362	2.755	1.00	18.32	A	O
ATOM	3611	N	LYS	A	640	23.319	-12.733	3.503	1.00	18.92	A	N
ATOM	3613	CA	LYS	A	640	24.431	-13.645	3.751	1.00	19.98	A	C
ATOM	3615	CB	LYS	A	640	25.777	-12.903	3.693	1.00	20.94	A	C
ATOM	3618	CG	LYS	A	640	26.233	-12.229	4.965	1.00	24.88	A	C
ATOM	3621	CD	LYS	A	640	27.432	-11.309	4.704	1.00	28.51	A	C
ATOM	3624	CE	LYS	A	640	28.699	-12.102	4.445	1.00	30.97	A	C
ATOM	3627	NZ	LYS	A	640	29.922	-11.339	4.842	1.00	32.88	A	N
ATOM	3631	C	LYS	A	640	24.244	-14.456	5.038	1.00	19.37	A	C
ATOM	3632	O	LYS	A	640	25.047	-15.343	5.324	1.00	20.32	A	O
ATOM	3633	N	GLY	A	641	23.172	-14.188	5.795	1.00	18.02	A	N
ATOM	3635	CA	GLY	A	641	22.864	-14.947	7.006	1.00	17.51	A	C
ATOM	3638	C	GLY	A	641	23.309	-14.328	8.324	1.00	16.94	A	C
ATOM	3639	O	GLY	A	641	23.063	-14.876	9.398	1.00	17.26	A	O
ATOM	3640	N	ASP	A	642	23.978	-13.186	8.260	1.00	15.83	A	N
ATOM	3642	CA	ASP	A	642	24.426	-12.516	9.476	1.00	15.01	A	C

ATOM	3644	CB	ASP	A	642	25.482	-11.476	9.155	1.00	15.19	A	C
ATOM	3647	CG	ASP	A	642	26.786	-12.079	8.651	1.00	18.80	A	C
ATOM	3648	OD1	ASP	A	642	27.065	-13.269	8.921	1.00	19.61	A	O
ATOM	3649	OD2	ASP	A	642	27.586	-11.400	7.975	1.00	23.88	A	O
ATOM	3650	C	ASP	A	642	23.249	-11.815	10.152	1.00	13.57	A	C
ATOM	3651	O	ASP	A	642	22.307	-11.354	9.490	1.00	12.33	A	O
ATOM	3652	N	ARG	A	643	23.362	-11.697	11.464	1.00	12.50	A	N
ATOM	3654	CA	ARG	A	643	22.331	-11.111	12.317	1.00	12.39	A	C
ATOM	3656	CB	ARG	A	643	21.489	-12.225	12.953	1.00	12.39	A	C
ATOM	3659	CG	ARG	A	643	20.694	-13.090	11.983	1.00	12.03	A	C
ATOM	3662	CD	ARG	A	643	19.623	-12.348	11.205	1.00	11.99	A	C
ATOM	3665	NE	ARG	A	643	18.815	-13.225	10.362	1.00	13.20	A	N
ATOM	3667	CZ	ARG	A	643	19.009	-13.447	9.066	1.00	12.12	A	C
ATOM	3668	NH1	ARG	A	643	20.017	-12.891	8.422	1.00	12.02	A	N
ATOM	3671	NH2	ARG	A	643	18.192	-14.246	8.407	1.00	13.42	A	N
ATOM	3674	C	ARG	A	643	22.971	-10.248	13.403	1.00	11.47	A	C
ATOM	3675	O	ARG	A	643	24.193	-10.287	13.620	1.00	12.13	A	O
ATOM	3676	N	LEU	A	644	22.153	-9.467	14.099	1.00	10.94	A	N
ATOM	3678	CA	LEU	A	644	22.594	-8.737	15.290	1.00	10.40	A	C
ATOM	3680	CB	LEU	A	644	21.419	-7.958	15.904	1.00	9.69	A	C
ATOM	3683	CG	LEU	A	644	20.852	-6.832	15.018	1.00	11.08	A	C
ATOM	3685	CD1	LEU	A	644	19.472	-6.365	15.508	1.00	9.53	A	C
ATOM	3689	CD2	LEU	A	644	21.813	-5.666	14.973	1.00	10.40	A	C
ATOM	3693	C	LEU	A	644	23.159	-9.720	16.313	1.00	10.18	A	C
ATOM	3694	O	LEU	A	644	22.586	-10.783	16.529	1.00	9.49	A	O
ATOM	3695	N	PRO	A	645	24.294	-9.404	16.929	1.00	11.40	A	N
ATOM	3696	CA	PRO	A	645	24.890	-10.317	17.908	1.00	11.04	A	C
ATOM	3698	CB	PRO	A	645	26.306	-9.773	18.072	1.00	11.53	A	C
ATOM	3701	CG	PRO	A	645	26.133	-8.323	17.893	1.00	12.78	A	C
ATOM	3704	CD	PRO	A	645	25.098	-8.180	16.770	1.00	11.64	A	C
ATOM	3707	C	PRO	A	645	24.153	-10.280	19.237	1.00	10.76	A	C
ATOM	3708	O	PRO	A	645	23.433	-9.317	19.545	1.00	10.19	A	O
ATOM	3709	N	LYS	A	646	24.334	-11.309	20.050	1.00	10.57	A	N
ATOM	3711	CA	LYS	A	646	23.713	-11.298	21.372	1.00	11.04	A	C
ATOM	3713	CB	LYS	A	646	23.920	-12.626	22.090	1.00	11.87	A	C
ATOM	3716	CG	LYS	A	646	23.106	-12.693	23.388	1.00	12.94	A	C
ATOM	3719	CD	LYS	A	646	23.208	-14.023	24.094	1.00	15.55	A	C
ATOM	3722	CE	LYS	A	646	24.549	-14.181	24.784	1.00	17.68	A	C
ATOM	3725	NZ	LYS	A	646	24.744	-13.211	25.909	1.00	17.61	A	N
ATOM	3729	C	LYS	A	646	24.245	-10.171	22.262	1.00	11.04	A	C
ATOM	3730	O	LYS	A	646	25.455	-10.098	22.512	1.00	10.00	A	O
ATOM	3731	N	PRO	A	647	23.367	-9.298	22.764	1.00	11.04	A	N
ATOM	3732	CA	PRO	A	647	23.795	-8.304	23.753	1.00	11.70	A	C
ATOM	3734	CB	PRO	A	647	22.493	-7.562	24.101	1.00	11.68	A	C
ATOM	3737	CG	PRO	A	647	21.613	-7.755	22.933	1.00	10.24	A	C
ATOM	3740	CD	PRO	A	647	21.939	-9.134	22.407	1.00	10.94	A	C
ATOM	3743	C	PRO	A	647	24.385	-9.009	24.989	1.00	12.95	A	C
ATOM	3744	O	PRO	A	647	23.903	-10.073	25.362	1.00	13.55	A	O
ATOM	3745	N	ASP	A	648	25.404	-8.419	25.596	1.00	14.13	A	N
ATOM	3747	CA	ASP	A	648	26.079	-9.025	26.746	1.00	15.83	A	C
ATOM	3749	CB	ASP	A	648	27.078	-8.037	27.343	1.00	16.30	A	C
ATOM	3752	CG	ASP	A	648	27.957	-8.685	28.387	1.00	19.77	A	C
ATOM	3753	OD1	ASP	A	648	28.581	-9.737	28.087	1.00	23.36	A	O
ATOM	3754	OD2	ASP	A	648	28.045	-8.239	29.538	1.00	22.83	A	O
ATOM	3755	C	ASP	A	648	25.132	-9.530	27.867	1.00	15.47	A	C
ATOM	3756	O	ASP	A	648	25.328	-10.620	28.405	1.00	15.60	A	O
ATOM	3757	N	LEU	A	649	24.107	-8.758	28.208	1.00	15.04	A	N
ATOM	3759	CA	LEU	A	649	23.198	-9.145	29.293	1.00	15.54	A	C
ATOM	3761	CB	LEU	A	649	22.786	-7.917	30.102	1.00	16.16	A	C
ATOM	3764	CG	LEU	A	649	23.972	-7.268	30.829	1.00	18.63	A	C
ATOM	3766	CD1	LEU	A	649	23.508	-6.172	31.752	1.00	21.84	A	C
ATOM	3770	CD2	LEU	A	649	24.819	-8.285	31.590	1.00	20.44	A	C
ATOM	3774	C	LEU	A	649	21.958	-9.928	28.864	1.00	15.26	A	C
ATOM	3775	O	LEU	A	649	21.143	-10.329	29.702	1.00	15.43	A	O
ATOM	3776	N	CYS	A	650	21.816	-10.172	27.573	1.00	14.41	A	N
ATOM	3778	CA	CYS	A	650	20.722	-10.976	27.078	1.00	14.24	A	C
ATOM	3780	CB	CYS	A	650	20.630	-10.821	25.562	1.00	14.58	A	C

ATOM	3783	SG	CYS	A	650	19.263	-11.720	24.860	1.00	14.34	A	S
ATOM	3784	C	CYS	A	650	20.886	-12.462	27.463	1.00	14.97	A	C
ATOM	3785	O	CYS	A	650	21.918	-13.062	27.147	1.00	14.59	A	O
ATOM	3786	N	PRO	A	651	19.882	-13.046	28.131	1.00	15.29	A	N
ATOM	3787	CA	PRO	A	651	19.881	-14.480	28.453	1.00	15.51	A	C
ATOM	3789	CB	PRO	A	651	18.505	-14.690	29.096	1.00	15.33	A	C
ATOM	3792	CG	PRO	A	651	18.118	-13.377	29.606	1.00	16.20	A	C
ATOM	3795	CD	PRO	A	651	18.647	-12.395	28.606	1.00	15.45	A	C
ATOM	3798	C	PRO	A	651	19.950	-15.280	27.156	1.00	15.61	A	C
ATOM	3799	O	PRO	A	651	19.232	-14.936	26.226	1.00	13.93	A	O
ATOM	3800	N	PRO	A	652	20.796	-16.304	27.069	1.00	15.46	A	N
ATOM	3801	CA	PRO	A	652	20.857	-17.144	25.865	1.00	15.22	A	C
ATOM	3803	CB	PRO	A	652	21.714	-18.328	26.322	1.00	16.43	A	C
ATOM	3806	CG	PRO	A	652	22.606	-17.704	27.397	1.00	15.77	A	C
ATOM	3809	CD	PRO	A	652	21.777	-16.707	28.093	1.00	16.56	A	C
ATOM	3812	C	PRO	A	652	19.492	-17.602	25.303	1.00	14.66	A	C
ATOM	3813	O	PRO	A	652	19.290	-17.564	24.078	1.00	13.44	A	O
ATOM	3814	N	VAL	A	653	18.583	-18.024	26.175	1.00	14.07	A	N
ATOM	3816	CA	VAL	A	653	17.232	-18.429	25.766	1.00	14.45	A	C
ATOM	3818	CB	VAL	A	653	16.422	-18.968	26.990	1.00	15.04	A	C
ATOM	3820	CG1	VAL	A	653	16.178	-17.897	28.039	1.00	16.41	A	C
ATOM	3824	CG2	VAL	A	653	15.103	-19.588	26.565	1.00	16.73	A	C
ATOM	3828	C	VAL	A	653	16.476	-17.297	25.056	1.00	13.12	A	C
ATOM	3829	O	VAL	A	653	15.724	-17.519	24.101	1.00	13.27	A	O
ATOM	3830	N	LEU	A	654	16.671	-16.075	25.525	1.00	12.25	A	N
ATOM	3832	CA	LEU	A	654	16.061	-14.930	24.859	1.00	11.55	A	C
ATOM	3834	CB	LEU	A	654	16.133	-13.699	25.762	1.00	12.25	A	C
ATOM	3837	CG	LEU	A	654	15.424	-12.465	25.211	1.00	11.73	A	C
ATOM	3839	CD1	LEU	A	654	13.992	-12.763	24.836	1.00	12.71	A	C
ATOM	3843	CD2	LEU	A	654	15.497	-11.336	26.213	1.00	15.67	A	C
ATOM	3847	C	LEU	A	654	16.705	-14.659	23.499	1.00	11.43	A	C
ATOM	3848	O	LEU	A	654	16.017	-14.299	22.532	1.00	9.70	A	O
ATOM	3849	N	TYR	A	655	18.023	-14.819	23.391	1.00	10.65	A	N
ATOM	3851	CA	TYR	A	655	18.650	-14.626	22.089	1.00	10.82	A	C
ATOM	3853	CB	TYR	A	655	20.170	-14.605	22.197	1.00	10.18	A	C
ATOM	3856	CG	TYR	A	655	20.847	-14.244	20.909	1.00	10.71	A	C
ATOM	3857	CD1	TYR	A	655	20.691	-12.978	20.344	1.00	9.23	A	C
ATOM	3859	CE1	TYR	A	655	21.328	-12.648	19.126	1.00	10.02	A	C
ATOM	3861	CZ	TYR	A	655	22.107	-13.582	18.493	1.00	10.45	A	C
ATOM	3862	OH	TYR	A	655	22.732	-13.275	17.313	1.00	11.48	A	O
ATOM	3864	CE2	TYR	A	655	22.257	-14.848	19.030	1.00	11.87	A	C
ATOM	3866	CD2	TYR	A	655	21.607	-15.175	20.222	1.00	11.48	A	C
ATOM	3868	C	TYR	A	655	18.159	-15.669	21.083	1.00	11.69	A	C
ATOM	3869	O	TYR	A	655	17.945	-15.356	19.924	1.00	13.15	A	O
ATOM	3870	N	THR	A	656	17.913	-16.896	21.538	1.00	12.50	A	N
ATOM	3872	CA	THR	A	656	17.343	-17.927	20.681	1.00	12.57	A	C
ATOM	3874	CB	THR	A	656	17.203	-19.233	21.454	1.00	12.96	A	C
ATOM	3876	OG1	THR	A	656	18.524	-19.752	21.709	1.00	13.90	A	O
ATOM	3878	CG2	THR	A	656	16.497	-20.292	20.634	1.00	13.68	A	C
ATOM	3882	C	THR	A	656	16.002	-17.478	20.123	1.00	12.60	A	C
ATOM	3883	O	THR	A	656	15.725	-17.642	18.942	1.00	12.69	A	O
ATOM	3884	N	LEU	A	657	15.196	-16.876	20.968	1.00	12.41	A	N
ATOM	3886	CA	LEU	A	657	13.896	-16.387	20.550	1.00	13.31	A	C
ATOM	3888	CB	LEU	A	657	13.159	-15.855	21.767	1.00	13.71	A	C
ATOM	3891	CG	LEU	A	657	11.651	-15.834	21.701	1.00	17.10	A	C
ATOM	3893	CD1	LEU	A	657	11.129	-17.245	21.475	1.00	17.52	A	C
ATOM	3897	CD2	LEU	A	657	11.093	-15.233	22.999	1.00	17.71	A	C
ATOM	3901	C	LEU	A	657	14.035	-15.306	19.478	1.00	12.69	A	C
ATOM	3902	O	LEU	A	657	13.318	-15.328	18.471	1.00	11.85	A	O
ATOM	3903	N	MET	A	658	14.973	-14.381	19.681	1.00	12.08	A	N
ATOM	3905	CA	MET	A	658	15.256	-13.329	18.704	1.00	12.19	A	C
ATOM	3907	CB	MET	A	658	16.394	-12.406	19.158	1.00	12.40	A	C
ATOM	3910	CG	MET	A	658	16.108	-11.534	20.375	1.00	14.24	A	C
ATOM	3913	SD	MET	A	658	17.644	-10.690	20.859	1.00	17.59	A	S
ATOM	3914	CE	MET	A	658	17.109	-9.824	22.311	1.00	17.80	A	C
ATOM	3918	C	MET	A	658	15.622	-13.928	17.361	1.00	11.84	A	C
ATOM	3919	O	MET	A	658	15.138	-13.476	16.317	1.00	11.75	A	O

ATOM	3920	N	THR	A	659	16.467	-14.964	17.370	1.00	11.94	A	N
ATOM	3922	CA	THR	A	659	16.955	-15.520	16.113	1.00	12.12	A	C
ATOM	3924	CB	THR	A	659	18.149	-16.515	16.292	1.00	12.54	A	C
ATOM	3926	OG1	THR	A	659	17.762	-17.627	17.096	1.00	16.72	A	O
ATOM	3928	CG2	THR	A	659	19.287	-15.907	17.045	1.00	12.86	A	C
ATOM	3932	C	THR	A	659	15.821	-16.169	15.321	1.00	11.44	A	C
ATOM	3933	O	THR	A	659	15.857	-16.155	14.085	1.00	11.07	A	O
ATOM	3934	N	ARG	A	660	14.828	-16.730	16.026	1.00	11.23	A	N
ATOM	3936	CA	ARG	A	660	13.648	-17.313	15.390	1.00	11.85	A	C
ATOM	3938	CB	ARG	A	660	12.801	-18.090	16.395	1.00	12.33	A	C
ATOM	3941	CG	ARG	A	660	13.442	-19.396	16.829	1.00	15.41	A	C
ATOM	3944	CD	ARG	A	660	12.668	-20.082	17.920	1.00	18.66	A	C
ATOM	3947	NE	ARG	A	660	11.342	-20.465	17.435	1.00	21.96	A	N
ATOM	3949	CZ	ARG	A	660	10.238	-20.507	18.175	1.00	24.62	A	C
ATOM	3950	NH1	ARG	A	660	10.262	-20.224	19.484	1.00	25.28	A	N
ATOM	3953	NH2	ARG	A	660	9.104	-20.872	17.604	1.00	25.04	A	N
ATOM	3956	C	ARG	A	660	12.790	-16.249	14.711	1.00	11.14	A	C
ATOM	3957	O	ARG	A	660	12.256	-16.473	13.614	1.00	11.17	A	O
ATOM	3958	N	CYS	A	661	12.695	-15.082	15.345	1.00	10.45	A	N
ATOM	3960	CA	CYS	A	661	12.009	-13.926	14.756	1.00	10.32	A	C
ATOM	3962	CB	CYS	A	661	11.839	-12.812	15.791	1.00	10.37	A	C
ATOM	3965	SG	CYS	A	661	10.842	-13.203	17.247	1.00	11.06	A	S
ATOM	3966	C	CYS	A	661	12.729	-13.350	13.538	1.00	10.43	A	C
ATOM	3967	O	CYS	A	661	12.100	-12.678	12.705	1.00	10.50	A	O
ATOM	3968	N	TRP	A	662	14.036	-13.597	13.427	1.00	9.89	A	N
ATOM	3970	CA	TRP	A	662	14.812	-13.171	12.269	1.00	9.87	A	C
ATOM	3972	CB	TRP	A	662	16.154	-12.573	12.706	1.00	9.96	A	C
ATOM	3975	CG	TRP	A	662	16.045	-11.379	13.624	1.00	7.99	A	C
ATOM	3976	CD1	TRP	A	662	15.098	-10.395	13.601	1.00	9.64	A	C
ATOM	3978	NE1	TRP	A	662	15.341	-9.479	14.599	1.00	9.65	A	N
ATOM	3980	CE2	TRP	A	662	16.458	-9.867	15.292	1.00	9.01	A	C
ATOM	3981	CD2	TRP	A	662	16.915	-11.064	14.707	1.00	8.52	A	C
ATOM	3982	CE3	TRP	A	662	18.060	-11.668	15.241	1.00	8.33	A	C
ATOM	3984	CZ3	TRP	A	662	18.678	-11.079	16.328	1.00	9.97	A	C
ATOM	3986	CH2	TRP	A	662	18.197	-9.903	16.882	1.00	9.90	A	C
ATOM	3988	CZ2	TRP	A	662	17.091	-9.285	16.390	1.00	8.65	A	C
ATOM	3990	C	TRP	A	662	15.035	-14.293	11.250	1.00	10.88	A	C
ATOM	3991	O	TRP	A	662	16.003	-14.279	10.518	1.00	11.46	A	O
ATOM	3992	N	ASP	A	663	14.117	-15.247	11.169	1.00	12.36	A	N
ATOM	3994	CA	ASP	A	663	14.145	-16.205	10.079	1.00	13.31	A	C
ATOM	3996	CB	ASP	A	663	13.079	-17.269	10.250	1.00	13.47	A	C
ATOM	3999	CG	ASP	A	663	13.383	-18.523	9.450	1.00	17.38	A	C
ATOM	4000	OD1	ASP	A	663	13.368	-18.472	8.199	1.00	19.87	A	O
ATOM	4001	OD2	ASP	A	663	13.623	-19.611	10.004	1.00	19.38	A	O
ATOM	4002	C	ASP	A	663	13.902	-15.428	8.791	1.00	13.36	A	C
ATOM	4003	O	ASP	A	663	13.021	-14.564	8.740	1.00	12.27	A	O
ATOM	4004	N	TYR	A	664	14.708	-15.693	7.772	1.00	13.88	A	N
ATOM	4006	CA	TYR	A	664	14.563	-14.999	6.493	1.00	14.75	A	C
ATOM	4008	CB	TYR	A	664	15.586	-15.465	5.445	1.00	15.39	A	C
ATOM	4011	CG	TYR	A	664	15.757	-14.437	4.351	1.00	16.86	A	C
ATOM	4012	CD1	TYR	A	664	16.650	-13.378	4.508	1.00	19.69	A	C
ATOM	4014	CE1	TYR	A	664	16.807	-12.418	3.526	1.00	21.35	A	C
ATOM	4016	CZ	TYR	A	664	16.055	-12.492	2.381	1.00	21.53	A	C
ATOM	4017	OH	TYR	A	664	16.230	-11.512	1.432	1.00	26.28	A	O
ATOM	4019	CE2	TYR	A	664	15.146	-13.520	2.189	1.00	21.81	A	C
ATOM	4021	CD2	TYR	A	664	14.992	-14.490	3.181	1.00	19.31	A	C
ATOM	4023	C	TYR	A	664	13.158	-15.162	5.918	1.00	15.14	A	C
ATOM	4024	O	TYR	A	664	12.615	-14.215	5.389	1.00	15.70	A	O
ATOM	4025	N	ASP	A	665	12.602	-16.366	6.020	1.00	15.67	A	N
ATOM	4027	CA	ASP	A	665	11.266	-16.674	5.507	1.00	16.37	A	C
ATOM	4029	CB	ASP	A	665	11.137	-18.185	5.297	1.00	16.98	A	C
ATOM	4032	CG	ASP	A	665	9.894	-18.570	4.536	1.00	20.27	A	C
ATOM	4033	OD1	ASP	A	665	8.880	-17.841	4.603	1.00	21.22	A	O
ATOM	4034	OD2	ASP	A	665	9.847	-19.600	3.828	1.00	25.29	A	O
ATOM	4035	C	ASP	A	665	10.197	-16.222	6.508	1.00	15.72	A	C
ATOM	4036	O	ASP	A	665	10.133	-16.769	7.607	1.00	14.51	A	O
ATOM	4037	N	PRO	A	666	9.382	-15.230	6.167	1.00	16.24	A	N

ATOM	4038	CA	PRO	A	666	8.375	-14.747	7.129	1.00	16.93	A	C
ATOM	4040	CB	PRO	A	666	7.583	-13.690	6.346	1.00	17.41	A	C
ATOM	4043	CG	PRO	A	666	8.026	-13.812	4.904	1.00	17.55	A	C
ATOM	4046	CD	PRO	A	666	9.371	-14.460	4.914	1.00	16.23	A	C
ATOM	4049	C	PRO	A	666	7.471	-15.869	7.673	1.00	17.49	A	C
ATOM	4050	O	PRO	A	666	7.117	-15.846	8.857	1.00	16.21	A	O
ATOM	4051	N	SER	A	667	7.161	-16.855	6.823	1.00	18.52	A	N
ATOM	4053	CA	SER	A	667	6.277	-17.980	7.182	1.00	19.22	A	C
ATOM	4055	CB	SER	A	667	6.089	-18.936	5.988	1.00	19.21	A	C
ATOM	4058	OG	SER	A	667	5.265	-18.349	5.018	1.00	22.33	A	O
ATOM	4060	C	SER	A	667	6.774	-18.786	8.355	1.00	18.58	A	C
ATOM	4061	O	SER	A	667	5.977	-19.427	9.028	1.00	19.88	A	O
ATOM	4062	N	ASP	A	668	8.083	-18.767	8.602	1.00	18.14	A	N
ATOM	4064	CA	ASP	A	668	8.691	-19.514	9.690	1.00	17.77	A	C
ATOM	4066	CB	ASP	A	668	10.041	-20.074	9.239	1.00	18.75	A	C
ATOM	4069	CG	ASP	A	668	9.875	-21.107	8.141	1.00	22.03	A	C
ATOM	4070	OD1	ASP	A	668	10.883	-21.598	7.597	1.00	27.40	A	O
ATOM	4071	OD2	ASP	A	668	8.741	-21.464	7.754	1.00	25.19	A	O
ATOM	4072	C	ASP	A	668	8.866	-18.773	10.999	1.00	16.19	A	C
ATOM	4073	O	ASP	A	668	9.285	-19.368	11.975	1.00	16.42	A	O
ATOM	4074	N	ARG	A	669	8.544	-17.484	11.041	1.00	14.15	A	N
ATOM	4076	CA	ARG	A	669	8.698	-16.742	12.294	1.00	12.17	A	C
ATOM	4078	CB	ARG	A	669	8.754	-15.241	12.032	1.00	11.55	A	C
ATOM	4081	CG	ARG	A	669	9.876	-14.823	11.139	1.00	10.93	A	C
ATOM	4084	CD	ARG	A	669	9.765	-13.404	10.667	1.00	8.98	A	C
ATOM	4087	NE	ARG	A	669	10.697	-13.209	9.551	1.00	9.01	A	N
ATOM	4089	CZ	ARG	A	669	10.533	-12.298	8.608	1.00	8.74	A	C
ATOM	4090	NH1	ARG	A	669	9.534	-11.433	8.687	1.00	9.38	A	N
ATOM	4093	NH2	ARG	A	669	11.399	-12.224	7.601	1.00	9.94	A	N
ATOM	4096	C	ARG	A	669	7.528	-17.054	13.223	1.00	11.87	A	C
ATOM	4097	O	ARG	A	669	6.428	-17.374	12.748	1.00	11.94	A	O
ATOM	4098	N	PRO	A	670	7.721	-16.936	14.531	1.00	11.24	A	N
ATOM	4099	CA	PRO	A	670	6.624	-17.164	15.492	1.00	10.97	A	C
ATOM	4101	CB	PRO	A	670	7.294	-16.965	16.857	1.00	12.04	A	C
ATOM	4104	CG	PRO	A	670	8.752	-16.960	16.597	1.00	12.70	A	C
ATOM	4107	CD	PRO	A	670	8.967	-16.549	15.200	1.00	11.74	A	C
ATOM	4110	C	PRO	A	670	5.502	-16.141	15.365	1.00	10.78	A	C
ATOM	4111	O	PRO	A	670	5.748	-15.057	14.862	1.00	10.11	A	O
ATOM	4112	N	ARG	A	671	4.306	-16.486	15.841	1.00	10.15	A	N
ATOM	4114	CA	ARG	A	671	3.225	-15.531	16.041	1.00	10.66	A	C
ATOM	4116	CB	ARG	A	671	1.913	-16.274	16.265	1.00	11.28	A	C
ATOM	4119	CG	ARG	A	671	1.425	-17.188	15.162	1.00	14.40	A	C
ATOM	4122	CD	ARG	A	671	0.097	-17.817	15.566	1.00	18.14	A	C
ATOM	4125	NE	ARG	A	671	-0.602	-18.573	14.531	1.00	19.61	A	N
ATOM	4127	CZ	ARG	A	671	-0.460	-19.884	14.309	1.00	22.54	A	C
ATOM	4128	NH1	ARG	A	671	0.379	-20.617	15.035	1.00	21.69	A	N
ATOM	4131	NH2	ARG	A	671	-1.180	-20.473	13.358	1.00	23.16	A	N
ATOM	4134	C	ARG	A	671	3.478	-14.710	17.304	1.00	9.70	A	C
ATOM	4135	O	ARG	A	671	4.179	-15.161	18.193	1.00	9.46	A	O
ATOM	4136	N	PHE	A	672	2.854	-13.549	17.425	1.00	9.68	A	N
ATOM	4138	CA	PHE	A	672	2.954	-12.793	18.661	1.00	9.83	A	C
ATOM	4140	CB	PHE	A	672	2.376	-11.377	18.529	1.00	9.02	A	C
ATOM	4143	CG	PHE	A	672	3.314	-10.400	17.874	1.00	7.29	A	C
ATOM	4144	CD1	PHE	A	672	4.499	-10.034	18.499	1.00	7.29	A	C
ATOM	4146	CE1	PHE	A	672	5.348	-9.114	17.899	1.00	6.39	A	C
ATOM	4148	CZ	PHE	A	672	5.024	-8.548	16.678	1.00	6.43	A	C
ATOM	4150	CE2	PHE	A	672	3.873	-8.906	16.040	1.00	7.92	A	C
ATOM	4152	CD2	PHE	A	672	3.008	-9.841	16.639	1.00	7.47	A	C
ATOM	4154	C	PHE	A	672	2.316	-13.516	19.857	1.00	10.52	A	C
ATOM	4155	O	PHE	A	672	2.809	-13.376	20.963	1.00	10.42	A	O
ATOM	4156	N	THR	A	673	1.245	-14.285	19.652	1.00	11.02	A	N
ATOM	4158	CA	THR	A	673	0.664	-15.049	20.764	1.00	12.24	A	C
ATOM	4160	CB	THR	A	673	-0.597	-15.834	20.351	1.00	12.82	A	C
ATOM	4162	OG1	THR	A	673	-0.322	-16.642	19.189	1.00	13.06	A	O
ATOM	4164	CG2	THR	A	673	-1.684	-14.908	19.961	1.00	14.88	A	C
ATOM	4168	C	THR	A	673	1.682	-16.025	21.330	1.00	12.24	A	C
ATOM	4169	O	THR	A	673	1.768	-16.205	22.552	1.00	13.08	A	O

ATOM	4170	N	GLU	A	674	2.448	-16.653	20.435	1.00	11.03	A	N
ATOM	4172	CA	GLU	A	674	3.482	-17.598	20.811	1.00	11.45	A	C
ATOM	4174	CB	GLU	A	674	3.971	-18.366	19.575	1.00	11.48	A	C
ATOM	4177	CG	GLU	A	674	2.851	-19.201	18.944	1.00	12.48	A	C
ATOM	4180	CD	GLU	A	674	3.143	-19.750	17.549	1.00	17.12	A	C
ATOM	4181	OE1	GLU	A	674	4.096	-19.296	16.881	1.00	15.46	A	O
ATOM	4182	OE2	GLU	A	674	2.370	-20.657	17.120	1.00	18.19	A	O
ATOM	4183	C	GLU	A	674	4.651	-16.904	21.527	1.00	11.40	A	C
ATOM	4184	O	GLU	A	674	5.194	-17.429	22.504	1.00	12.34	A	O
ATOM	4185	N	LEU	A	675	5.006	-15.714	21.070	1.00	11.03	A	N
ATOM	4187	CA	LEU	A	675	6.064	-14.951	21.712	1.00	10.62	A	C
ATOM	4189	CB	LEU	A	675	6.459	-13.750	20.855	1.00	10.87	A	C
ATOM	4192	CG	LEU	A	675	7.212	-14.093	19.574	1.00	11.12	A	C
ATOM	4194	CD1	LEU	A	675	7.279	-12.885	18.652	1.00	11.98	A	C
ATOM	4198	CD2	LEU	A	675	8.608	-14.669	19.883	1.00	12.08	A	C
ATOM	4202	C	LEU	A	675	5.674	-14.489	23.125	1.00	10.64	A	C
ATOM	4203	O	LEU	A	675	6.537	-14.412	23.997	1.00	10.13	A	O
ATOM	4204	N	VAL	A	676	4.401	-14.147	23.340	1.00	10.75	A	N
ATOM	4206	CA	VAL	A	676	3.949	-13.746	24.663	1.00	10.97	A	C
ATOM	4208	CB	VAL	A	676	2.481	-13.353	24.703	1.00	11.26	A	C
ATOM	4210	CG1	VAL	A	676	1.972	-13.247	26.176	1.00	11.67	A	C
ATOM	4214	CG2	VAL	A	676	2.265	-12.044	23.975	1.00	11.71	A	C
ATOM	4218	C	VAL	A	676	4.193	-14.922	25.623	1.00	12.06	A	C
ATOM	4219	O	VAL	A	676	4.724	-14.750	26.719	1.00	11.23	A	O
ATOM	4220	N	CYS	A	677	3.827	-16.118	25.189	1.00	12.77	A	N
ATOM	4222	CA	CYS	A	677	4.070	-17.309	26.003	1.00	13.59	A	C
ATOM	4224	CB	CYS	A	677	3.486	-18.526	25.322	1.00	14.78	A	C
ATOM	4227	SG	CYS	A	677	1.727	-18.420	25.306	1.00	23.73	A	S
ATOM	4228	C	CYS	A	677	5.544	-17.543	26.310	1.00	12.70	A	C
ATOM	4229	O	CYS	A	677	5.911	-17.813	27.472	1.00	12.44	A	O
ATOM	4230	N	SER	A	678	6.384	-17.449	25.280	1.00	10.95	A	N
ATOM	4232	CA	SER	A	678	7.809	-17.673	25.412	1.00	11.22	A	C
ATOM	4234	CB	SER	A	678	8.501	-17.631	24.052	1.00	11.49	A	C
ATOM	4237	OG	SER	A	678	8.087	-18.690	23.218	1.00	12.71	A	O
ATOM	4239	C	SER	A	678	8.463	-16.617	26.319	1.00	10.73	A	C
ATOM	4240	O	SER	A	678	9.291	-16.946	27.175	1.00	10.09	A	O
ATOM	4241	N	LEU	A	679	8.075	-15.359	26.131	1.00	10.12	A	N
ATOM	4243	CA	LEU	A	679	8.633	-14.277	26.941	1.00	10.19	A	C
ATOM	4245	CB	LEU	A	679	8.272	-12.920	26.386	1.00	10.05	A	C
ATOM	4248	CG	LEU	A	679	9.120	-12.519	25.180	1.00	10.35	A	C
ATOM	4250	CD1	LEU	A	679	8.594	-11.187	24.639	1.00	10.06	A	C
ATOM	4254	CD2	LEU	A	679	10.583	-12.406	25.546	1.00	13.61	A	C
ATOM	4258	C	LEU	A	679	8.185	-14.379	28.400	1.00	10.85	A	C
ATOM	4259	O	LEU	A	679	8.975	-14.105	29.293	1.00	10.86	A	O
ATOM	4260	N	SER	A	680	6.944	-14.812	28.632	1.00	11.33	A	N
ATOM	4262	CA	SER	A	680	6.442	-15.009	29.976	1.00	11.30	A	C
ATOM	4264	CB	SER	A	680	4.975	-15.458	29.955	1.00	11.82	A	C
ATOM	4267	OG	SER	A	680	4.160	-14.393	29.529	1.00	13.70	A	O
ATOM	4269	C	SER	A	680	7.294	-16.054	30.696	1.00	11.10	A	C
ATOM	4270	O	SER	A	680	7.569	-15.914	31.876	1.00	10.06	A	O
ATOM	4271	N	ASP	A	681	7.709	-17.079	29.965	1.00	11.27	A	N
ATOM	4273	CA	ASP	A	681	8.555	-18.151	30.489	1.00	11.79	A	C
ATOM	4275	CB	ASP	A	681	8.582	-19.302	29.480	1.00	12.73	A	C
ATOM	4278	CG	ASP	A	681	9.205	-20.567	30.017	1.00	16.09	A	C
ATOM	4279	OD1	ASP	A	681	9.063	-20.869	31.226	1.00	18.24	A	O
ATOM	4280	OD2	ASP	A	681	9.823	-21.351	29.260	1.00	19.49	A	O
ATOM	4281	C	ASP	A	681	9.962	-17.637	30.793	1.00	11.36	A	C
ATOM	4282	O	ASP	A	681	10.524	-17.962	31.832	1.00	10.57	A	O
ATOM	4283	N	VAL	A	682	10.514	-16.805	29.911	1.00	10.17	A	N
ATOM	4285	CA	VAL	A	682	11.831	-16.189	30.137	1.00	10.71	A	C
ATOM	4287	CB	VAL	A	682	12.323	-15.421	28.879	1.00	11.06	A	C
ATOM	4289	CG1	VAL	A	682	13.585	-14.610	29.186	1.00	13.37	A	C
ATOM	4293	CG2	VAL	A	682	12.586	-16.394	27.719	1.00	12.19	A	C
ATOM	4297	C	VAL	A	682	11.784	-15.270	31.371	1.00	10.10	A	C
ATOM	4298	O	VAL	A	682	12.698	-15.271	32.194	1.00	9.87	A	O
ATOM	4299	N	TYR	A	683	10.713	-14.501	31.498	1.00	9.76	A	N
ATOM	4301	CA	TYR	A	683	10.535	-13.588	32.615	1.00	10.41	A	C

ATOM	4303	CB	TYR	A	683	9.258	-12.801	32.428	1.00	10.16	A	C
ATOM	4306	CG	TYR	A	683	8.986	-11.749	33.480	1.00	11.77	A	C
ATOM	4307	CD1	TYR	A	683	9.973	-10.837	33.858	1.00	12.15	A	C
ATOM	4309	CE1	TYR	A	683	9.719	-9.862	34.816	1.00	14.98	A	C
ATOM	4311	CZ	TYR	A	683	8.480	-9.787	35.386	1.00	15.15	A	C
ATOM	4312	OH	TYR	A	683	8.225	-8.818	36.312	1.00	16.29	A	O
ATOM	4314	CE2	TYR	A	683	7.477	-10.669	35.022	1.00	16.42	A	C
ATOM	4316	CD2	TYR	A	683	7.743	-11.648	34.070	1.00	13.80	A	C
ATOM	4318	C	TYR	A	683	10.482	-14.356	33.933	1.00	10.77	A	C
ATOM	4319	O	TYR	A	683	11.155	-13.994	34.896	1.00	10.66	A	O
ATOM	4320	N	GLN	A	684	9.701	-15.438	33.952	1.00	11.00	A	N
ATOM	4322	CA	GLN	A	684	9.618	-16.300	35.132	1.00	11.22	A	C
ATOM	4324	CB	GLN	A	684	8.629	-17.444	34.930	1.00	11.31	A	C
ATOM	4327	CG	GLN	A	684	8.375	-18.269	36.236	1.00	13.65	A	C
ATOM	4330	CD	GLN	A	684	7.820	-17.402	37.374	1.00	15.94	A	C
ATOM	4331	OE1	GLN	A	684	8.477	-17.197	38.403	1.00	19.21	A	O
ATOM	4332	NE2	GLN	A	684	6.630	-16.887	37.180	1.00	16.15	A	N
ATOM	4335	C	GLN	A	684	10.971	-16.890	35.468	1.00	11.59	A	C
ATOM	4336	O	GLN	A	684	11.344	-16.943	36.636	1.00	11.70	A	O
ATOM	4337	N	MET	A	685	11.690	-17.356	34.453	1.00	12.42	A	N
ATOM	4339	CA	MET	A	685	13.022	-17.913	34.646	1.00	14.85	A	C
ATOM	4341	CB	MET	A	685	13.616	-18.457	33.334	1.00	15.51	A	C
ATOM	4344	CG	MET	A	685	15.075	-18.894	33.413	1.00	20.31	A	C
ATOM	4347	SD	MET	A	685	16.347	-17.557	33.428	1.00	30.38	A	S
ATOM	4348	CE	MET	A	685	16.971	-17.643	31.702	1.00	29.94	A	C
ATOM	4352	C	MET	A	685	13.952	-16.870	35.251	1.00	14.79	A	C
ATOM	4353	O	MET	A	685	14.707	-17.201	36.149	1.00	14.67	A	O
ATOM	4354	N	GLU	A	686	13.908	-15.623	34.767	1.00	15.09	A	N
ATOM	4356	CA	GLU	A	686	14.782	-14.564	35.321	1.00	15.60	A	C
ATOM	4358	CB	GLU	A	686	14.765	-13.293	34.457	1.00	15.66	A	C
ATOM	4361	CG	GLU	A	686	15.520	-13.394	33.143	1.00	18.58	A	C
ATOM	4364	CD	GLU	A	686	17.018	-13.650	33.305	1.00	19.75	A	C
ATOM	4365	OE1	GLU	A	686	17.692	-12.967	34.110	1.00	19.12	A	O
ATOM	4366	OE2	GLU	A	686	17.521	-14.545	32.603	1.00	25.71	A	O
ATOM	4367	C	GLU	A	686	14.431	-14.212	36.776	1.00	15.84	A	C
ATOM	4368	O	GLU	A	686	15.319	-13.886	37.568	1.00	15.94	A	O
ATOM	4369	N	LYS	A	687	13.146	-14.251	37.124	1.00	15.72	A	N
ATOM	4371	CA	LYS	A	687	12.727	-14.031	38.499	1.00	16.97	A	C
ATOM	4373	CB	LYS	A	687	11.206	-13.895	38.594	1.00	16.88	A	C
ATOM	4376	CG	LYS	A	687	10.707	-12.578	38.036	1.00	17.92	A	C
ATOM	4379	CD	LYS	A	687	9.303	-12.243	38.452	1.00	19.62	A	C
ATOM	4382	CE	LYS	A	687	8.270	-13.060	37.692	1.00	20.81	A	C
ATOM	4385	NZ	LYS	A	687	6.878	-12.646	38.085	1.00	20.18	A	N
ATOM	4389	C	LYS	A	687	13.225	-15.171	39.407	1.00	17.45	A	C
ATOM	4390	O	LYS	A	687	13.629	-14.925	40.534	1.00	18.25	A	O
ATOM	4391	N	ASP	A	688	13.214	-16.399	38.900	1.00	18.00	A	N
ATOM	4393	CA	ASP	A	688	13.607	-17.573	39.679	1.00	19.39	A	C
ATOM	4395	CB	ASP	A	688	13.129	-18.859	38.991	1.00	19.60	A	C
ATOM	4398	CG	ASP	A	688	11.616	-19.005	39.009	1.00	20.07	A	C
ATOM	4399	OD1	ASP	A	688	10.939	-18.210	39.683	1.00	18.55	A	O
ATOM	4400	OD2	ASP	A	688	11.017	-19.885	38.363	1.00	21.49	A	O
ATOM	4401	C	ASP	A	688	15.114	-17.677	39.938	1.00	20.75	A	C
ATOM	4402	O	ASP	A	688	15.519	-18.280	40.936	1.00	20.21	A	O
ATOM	4403	N	ILE	A	689	15.932	-17.094	39.064	1.00	22.34	A	N
ATOM	4405	CA	ILE	A	689	17.401	-17.136	39.206	1.00	24.85	A	C
ATOM	4407	CB	ILE	A	689	18.096	-17.337	37.831	1.00	25.22	A	C
ATOM	4409	CG1	ILE	A	689	18.027	-16.062	36.982	1.00	24.97	A	C
ATOM	4412	CD1	ILE	A	689	18.969	-16.063	35.816	1.00	26.04	A	C
ATOM	4416	CG2	ILE	A	689	17.485	-18.515	37.100	1.00	26.30	A	C
ATOM	4420	C	ILE	A	689	17.989	-15.894	39.845	1.00	26.98	A	C
ATOM	4421	O	ILE	A	689	19.220	-15.772	39.945	1.00	27.14	A	O
ATOM	4422	N	ALA	A	690	17.122	-14.964	40.247	1.00	29.52	A	N
ATOM	4424	CA	ALA	A	690	17.543	-13.708	40.840	1.00	31.03	A	C
ATOM	4426	CB	ALA	A	690	16.576	-12.605	40.460	1.00	31.13	A	C
ATOM	4430	C	ALA	A	690	17.629	-13.834	42.357	1.00	32.63	A	C
ATOM	4431	O	ALA	A	690	16.599	-13.900	43.042	1.00	32.75	A	O
ATOM	4432	N	MET	A	691	18.863	-13.859	42.864	1.00	34.71	A	N

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ATOM   4434  CA  MET A 691      19.159 -13.824  44.304  1.00 35.61      A    C
ATOM   4436  CB  MET A 691      18.556 -12.572  44.955  1.00 36.56      A    C
ATOM   4439  CG  MET A 691      19.081 -11.260  44.382  1.00 39.02      A    C
ATOM   4442  SD  MET A 691      18.165  -9.844  45.010  1.00 44.70      A    S
ATOM   4443  CE  MET A 691      16.654 -10.005  44.062  1.00 44.31      A    C
ATOM   4447  C   MET A 691      18.685 -15.085  45.012  1.00 35.54      A    C
ATOM   4448  O   MET A 691      18.582 -16.116  44.329  1.00 35.63      A    O
ATOM   4449  OXT MET A 691      18.437 -15.031  46.228  1.00 34.84      A    O
ATOM   4450  O1A ANP L   1       5.879  14.129  17.474  1.00 56.03      L    O
ATOM   4451  PA  ANP L   1       5.828  13.237  18.779  1.00 54.99      L    P
ATOM   4452  O2A ANP L   1       4.359  12.664  18.974  1.00 55.47      L    O
ATOM   4454  O3A ANP L   1       6.928  12.057  18.803  1.00 58.70      L    O
ATOM   4455  PB  ANP L   1       7.534  11.319  17.499  1.00 61.85      L    P
ATOM   4456  O1B ANP L   1       6.806  11.789  16.164  1.00 60.90      L    O
ATOM   4457  O2B ANP L   1       7.338   9.749  17.688  1.00 61.90      L    O
ATOM   4459  N3B ANP L   1       9.254  11.643  17.401  1.00 63.51      L    N
ATOM   4461  PG  ANP L   1       9.852  13.230  16.957  1.00 65.53      L    P
ATOM   4462  O3G ANP L   1      10.884  13.100  15.748  1.00 66.11      L    O
ATOM   4464  O2G ANP L   1      10.586  13.911  18.193  1.00 64.86      L    O
ATOM   4466  O1G ANP L   1       8.643  14.135  16.458  1.00 65.59      L    O
ATOM   4467  O5* ANP L   1       6.277  14.111  20.050  1.00 51.13      L    O
ATOM   4468  C5* ANP L   1       7.549  14.739  20.107  1.00 46.73      L    C
ATOM   4471  C4* ANP L   1       8.168  14.467  21.461  1.00 44.62      L    C
ATOM   4473  O4* ANP L   1       7.254  14.809  22.510  1.00 41.60      L    O
ATOM   4474  C1* ANP L   1       7.281  13.799  23.515  1.00 38.50      L    C
ATOM   4476  C2* ANP L   1       8.155  12.643  23.037  1.00 42.11      L    C
ATOM   4478  O2* ANP L   1       9.304  12.486  23.860  1.00 44.90      L    O
ATOM   4480  C3* ANP L   1       8.524  12.998  21.614  1.00 43.96      L    C
ATOM   4482  O3* ANP L   1       9.901  12.797  21.351  1.00 45.53      L    O
ATOM   4484  N9  ANP L   1       5.951  13.197  23.740  1.00 31.30      L    N
ATOM   4485  C8  ANP L   1       5.015  12.876  22.819  1.00 28.19      L    C
ATOM   4487  N7  ANP L   1       3.913  12.295  23.381  1.00 25.49      L    N
ATOM   4488  C5  ANP L   1       4.161  12.228  24.694  1.00 24.63      L    C
ATOM   4489  C6  ANP L   1       3.506  11.746  25.918  1.00 21.30      L    C
ATOM   4490  N6  ANP L   1       2.277  11.204  25.779  1.00 18.20      L    N
ATOM   4493  C4  ANP L   1       5.475  12.793  24.898  1.00 26.86      L    C
ATOM   4494  N3  ANP L   1       6.067  12.897  26.207  1.00 23.82      L    N
ATOM   4495  C2  ANP L   1       5.359  12.433  27.261  1.00 22.61      L    C
ATOM   4497  N1  ANP L   1       4.129  11.883  27.114  1.00 19.81      L    N
ATOM   4498  O   HOH M   1      11.906  10.877  19.048  1.00 54.80      M    O
ATOM   4501  O   HOH W   1      19.443  -9.552  13.290  1.00 12.78      W    O
ATOM   4504  O   HOH W   2      24.437  -5.004  22.245  1.00 16.30      W    O
ATOM   4507  O   HOH W   3      16.956  -5.546  11.116  1.00 14.32      W    O
ATOM   4510  O   HOH W   4      23.654  -5.882  27.256  1.00 16.76      W    O
ATOM   4513  O   HOH W   5      19.773  -2.500   2.719  1.00 17.82      W    O
ATOM   4516  O   HOH W   6      14.677   3.342  18.254  1.00 12.86      W    O
ATOM   4519  O   HOH W   7      15.460  -2.754  37.319  1.00 19.09      W    O
ATOM   4522  O   HOH W   8       0.917  -6.788  13.617  1.00 19.87      W    O
ATOM   4525  O   HOH W   9       6.262  -4.291   9.880  1.00 17.35      W    O
ATOM   4528  O   HOH W  10      -8.084  -9.594  20.676  1.00 19.55      W    O
ATOM   4531  O   HOH W  11       9.378  -6.760  37.711  1.00 23.16      W    O
ATOM   4534  O   HOH W  12      -4.324   2.362  25.030  1.00 17.21      W    O
ATOM   4537  O   HOH W  13       2.631  -4.978   2.213  1.00 21.67      W    O
ATOM   4540  O   HOH W  14      13.357   9.278  28.253  1.00 18.85      W    O
ATOM   4543  O   HOH W  15      18.009   2.532   9.354  1.00 17.12      W    O
ATOM   4546  O   HOH W  16      17.534  -9.551  37.009  1.00 20.96      W    O
ATOM   4549  O   HOH W  17      27.129  -8.112  21.598  1.00 20.80      W    O
ATOM   4552  O   HOH W  18      18.189 -15.606  12.347  1.00 21.79      W    O
ATOM   4555  O   HOH W  19      13.177   0.863  35.291  1.00 23.40      W    O
ATOM   4558  O   HOH W  20      17.054  -4.703   8.729  1.00 17.25      W    O
ATOM   4561  O   HOH W  21       7.866 -18.942  20.500  1.00 24.06      W    O
ATOM   4564  O   HOH W  22      14.700   7.035  22.806  1.00 16.93      W    O
ATOM   4567  O   HOH W  23      -2.679   2.607  28.131  1.00 23.11      W    O
ATOM   4570  O   HOH W  24       6.040  -9.803  37.824  1.00 33.92      W    O
ATOM   4573  O   HOH W  25      10.004  -5.316   9.507  1.00 23.61      W    O
ATOM   4576  O   HOH W  26      25.491  -5.320  24.819  1.00 23.18      W    O
ATOM   4579  O   HOH W  27       4.534  32.921  12.514  1.00 20.02      W    O
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ATOM   4582  O   HOH W  28      21.903 -11.752  31.783  1.00 27.60      W    O
ATOM   4585  O   HOH W  29      -2.817 -12.294  18.585  1.00 19.69      W    O
ATOM   4588  O   HOH W  30       0.619  25.243  18.899  1.00 22.14      W    O
ATOM   4591  O   HOH W  31       4.508  -2.772  -1.220  1.00 21.13      W    O
ATOM   4594  O   HOH W  32      26.872 -11.629  24.125  1.00 24.32      W    O
ATOM   4597  O   HOH W  33      26.063 -13.556  19.248  1.00 23.37      W    O
ATOM   4600  O   HOH W  34      -4.463  26.591  28.285  1.00 28.20      W    O
ATOM   4603  O   HOH W  35      -0.377  -9.432   8.082  1.00 25.76      W    O
ATOM   4606  O   HOH W  36      11.357   4.915  15.323  1.00 31.17      W    O
ATOM   4609  O   HOH W  37       0.444  -0.589   8.490  1.00 27.25      W    O
ATOM   4612  O   HOH W  38      12.025 -12.305   3.518  1.00 20.13      W    O
ATOM   4615  O   HOH W  39      -7.592  21.532  34.079  1.00 24.16      W    O
ATOM   4618  O   HOH W  40      -3.034  25.675  20.623  1.00 27.86      W    O
ATOM   4621  O   HOH W  41      19.252 -18.574  29.007  1.00 24.11      W    O
ATOM   4624  O   HOH W  42      18.447   5.050  22.545  1.00 26.98      W    O
ATOM   4627  O   HOH W  43      18.236   2.548  19.150  1.00 23.34      W    O
ATOM   4630  O   HOH W  44      23.599  -4.581   0.730  1.00 23.86      W    O
ATOM   4633  O   HOH W  45       5.670 -14.733  33.566  1.00 22.95      W    O
ATOM   4636  O   HOH W  46      14.080 -19.737  23.406  1.00 22.24      W    O
ATOM   4639  O   HOH W  47      22.734   4.890  34.891  1.00 26.97      W    O
ATOM   4642  O   HOH W  48      -3.602  22.418  16.052  1.00 29.22      W    O
ATOM   4645  O   HOH W  49      25.830 -12.392  15.030  1.00 32.70      W    O
ATOM   4648  O   HOH W  50      -2.320 -15.117  16.246  1.00 28.09      W    O
ATOM   4651  O   HOH W  51       2.614 -23.096  16.430  1.00 31.67      W    O
ATOM   4654  O   HOH W  52      17.362 -18.998  43.191  1.00 26.88      W    O
ATOM   4657  O   HOH W  53      26.474  -8.992  12.337  1.00 31.87      W    O
ATOM   4660  O   HOH W  54      16.830  -4.474  -1.805  1.00 36.41      W    O
ATOM   4663  O   HOH W  55       4.947  -4.071  36.311  1.00 25.83      W    O
ATOM   4666  O   HOH W  56       1.631   1.495  10.141  1.00 25.82      W    O
ATOM   4669  O   HOH W  57      21.157  -1.727  -0.971  1.00 32.21      W    O
ATOM   4672  O   HOH W  58      20.249  -8.173  36.530  1.00 21.67      W    O
ATOM   4675  O   HOH W  59      -2.610  -9.023   9.489  1.00 35.63      W    O
ATOM   4678  O   HOH W  60      -9.404  23.395  33.556  1.00 27.23      W    O
ATOM   4681  O   HOH W  61      11.153   3.802  -0.793  1.00 32.48      W    O
ATOM   4684  O   HOH W  62       2.156 -13.178  30.950  1.00 32.64      W    O
ATOM   4687  O   HOH W  63      15.393 -13.901  45.580  1.00 34.94      W    O
ATOM   4690  O   HOH W  64       5.734 -20.060  12.705  1.00 28.43      W    O
ATOM   4693  O   HOH W  65      -0.390  18.866   1.150  1.00 37.04      W    O
ATOM   4696  O   HOH W  66       9.308  23.821  20.537  1.00 33.19      W    O
ATOM   4699  O   HOH W  67      -8.657 -12.592  15.980  1.00 30.95      W    O
ATOM   4702  O   HOH W  68       6.009 -10.288   5.499  1.00 30.71      W    O
ATOM   4705  O   HOH W  69       5.849 -14.630  36.206  1.00 36.64      W    O
ATOM   4708  O   HOH W  70      -0.379 -15.926  24.303  1.00 26.34      W    O
ATOM   4711  O   HOH W  71      19.013   6.091  37.596  1.00 29.23      W    O
ATOM   4714  O   HOH W  72      -2.437  -8.935  24.621  1.00 26.00      W    O
ATOM   4717  O   HOH W  73      13.274  10.054   0.171  1.00 32.22      W    O
ATOM   4720  O   HOH W  74      11.266  -4.798  37.300  1.00 27.56      W    O
ATOM   4723  O   HOH W  75      18.634   5.650   3.509  1.00 30.22      W    O
ATOM   4726  O   HOH W  76      17.088 -17.411   8.048  1.00 26.93      W    O
ATOM   4729  O   HOH W  77      23.077   3.880   2.721  1.00 25.25      W    O
ATOM   4732  O   HOH W  78      24.631   5.289  28.100  1.00 53.16      W    O
ATOM   4735  O   HOH W  79      10.896  -4.046  -5.174  1.00 30.72      W    O
ATOM   4738  O   HOH W  80      21.483 -18.240  22.299  1.00 31.63      W    O
ATOM   4741  O   HOH W  81      17.664 -12.362  36.744  1.00 27.21      W    O
ATOM   4744  O   HOH W  82      -6.800  -5.096   9.419  1.00 31.32      W    O
ATOM   4747  O   HOH W  83       3.254  -6.214  33.543  1.00 29.36      W    O
ATOM   4750  O   HOH W  84      -6.655   5.297  23.427  1.00 38.97      W    O
ATOM   4753  O   HOH W  85       6.119   3.003   3.176  1.00 39.55      W    O
ATOM   4756  O   HOH W  86      16.440   5.449   7.469  1.00 35.83      W    O
ATOM   4759  O   HOH W  87      -6.743  15.088  41.223  1.00 33.66      W    O
ATOM   4762  O   HOH W  88      -8.714 -10.654  12.475  1.00 45.30      W    O
ATOM   4765  O   HOH W  89       5.455   6.147  14.560  1.00 34.25      W    O
ATOM   4768  O   HOH W  90       7.863  -2.178  41.320  1.00 41.21      W    O
ATOM   4771  O   HOH W  91       3.037  -8.511  31.787  1.00 43.98      W    O
ATOM   4774  O   HOH W  92      -5.700   2.904  27.490  1.00 30.78      W    O
ATOM   4777  O   HOH W  93      10.698 -16.094  41.240  1.00 40.42      W    O
ATOM   4780  O   HOH W  94       8.297 -21.654  26.890  1.00 35.50      W    O
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ATOM   4783  O   HOH W  95      -7.043  26.092  27.806  1.00 33.08      W    O
ATOM   4786  O   HOH W  96      12.953 -20.340  21.075  1.00 26.90      W    O
ATOM   4789  O   HOH W  97      -1.020   6.390  14.791  1.00 42.20      W    O
ATOM   4792  O   HOH W  98       9.903  -2.480  37.263  1.00 39.90      W    O
ATOM   4795  O   HOH W  99     -14.690   5.403  20.304  1.00 43.77      W    O
ATOM   4798  O   HOH W 100       7.497 -20.614  33.258  1.00 42.00      W    O
ATOM   4801  O   HOH W 101      -6.310  -0.802  28.924  1.00 38.73      W    O
ATOM   4804  O   HOH W 102      23.429   2.695  26.110  1.00 30.05      W    O
ATOM   4807  O   HOH W 103       5.939  23.666  15.058  1.00 45.24      W    O
ATOM   4810  O   HOH W 104      15.157  -8.657  41.812  1.00 48.42      W    O
ATOM   4813  O   HOH W 105      22.584   5.351   6.685  1.00 32.02      W    O
ATOM   4816  O   HOH W 106       1.947 -13.531  12.995  1.00 35.70      W    O
ATOM   4819  O   HOH W 107       0.843  -3.343   5.954  1.00 35.00      W    O
ATOM   4822  O   HOH W 108      10.764   8.978  -0.078  1.00 47.97      W    O
ATOM   4825  O   HOH W 109      12.609  11.593  33.799  1.00 33.88      W    O
ATOM   4828  O   HOH W 110      -2.559  28.085  29.916  1.00 40.24      W    O
ATOM   4831  O   HOH W 111      -8.695  -8.532   8.837  1.00 37.60      W    O
ATOM   4834  O   HOH W 112       1.265  18.134  33.506  1.00 37.44      W    O
ATOM   4837  O   HOH W 113      -9.981   6.869  11.619  1.00 38.18      W    O
ATOM   4840  O   HOH W 114      -2.744  14.784  38.949  1.00 50.37      W    O
ATOM   4843  O   HOH W 115      20.301 -12.723  34.212  1.00 40.49      W    O
ATOM   4846  O   HOH W 116      14.851   9.838  20.023  1.00 37.48      W    O
ATOM   4849  O   HOH W 117      23.651   3.698  39.134  1.00 37.78      W    O
ATOM   4852  O   HOH W 118     -18.557  13.257  30.128  1.00 41.89      W    O
ATOM   4855  O   HOH W 119      18.487 -21.421  23.859  1.00 39.29      W    O
ATOM   4858  O   HOH W 120      21.377   4.874  37.522  1.00 28.87      W    O
ATOM   4861  O   HOH W 121      18.415  -7.751  -2.248  1.00 36.44      W    O
ATOM   4864  O   HOH W 122      17.602  -7.842  12.411  1.00 16.38      W    O
ATOM   4867  O   HOH W 123      16.678   4.872  18.751  1.00 22.46      W    O
ATOM   4870  O   HOH W 124      14.066  -0.309  37.545  1.00 30.70      W    O
ATOM   4873  O   HOH W 125       7.740  -4.673  37.771  1.00 27.15      W    O
ATOM   4876  O   HOH W 126      13.728   4.405  15.630  1.00 25.76      W    O
ATOM   4879  O   HOH W 127      27.821  -6.501  23.920  1.00 31.77      W    O
ATOM   4882  O   HOH W 128      -3.928  27.852  25.640  1.00 29.97      W    O
ATOM   4885  O   HOH W 129      16.702   6.462  21.069  1.00 30.52      W    O
ATOM   4888  O   HOH W 130      26.185  -5.646  20.509  1.00 24.01      W    O
ATOM   4891  O   HOH W 131       1.974  -3.227   0.396  1.00 29.45      W    O
ATOM   4894  O   HOH W 132      18.503 -17.071  10.260  1.00 34.39      W    O
ATOM   4897  O   HOH W 133      10.397 -13.616   1.651  1.00 39.32      W    O
ATOM   4900  O   HOH W 134      -2.831  28.209  21.200  1.00 30.33      W    O
ATOM   4903  O   HOH W 135      15.320 -22.101  24.023  1.00 25.19      W    O
ATOM   4906  O   HOH W 136       4.007  -9.460  34.087  1.00 38.19      W    O
ATOM   4909  O   HOH W 137      -1.239 -11.368  25.339  1.00 28.01      W    O
ATOM   4912  O   HOH W 138      25.810 -13.282  12.651  1.00 29.26      W    O
ATOM   4915  O   HOH W 139     -11.471   3.486  23.719  1.00 43.71      W    O
ATOM   4918  O   HOH W 140     -14.572   6.189  16.547  1.00 32.73      W    O
ATOM   4921  O   HOH W 141      25.455  -4.517  28.979  1.00 27.27      W    O
ATOM   4924  O   HOH W 142      -2.265 -18.449  18.806  1.00 31.12      W    O
ATOM   4927  O   HOH W 143      24.881 -12.339  32.109  1.00 47.48      W    O
ATOM   4930  O   HOH W 144       3.783 -12.994  33.207  1.00 40.92      W    O
ATOM   4933  O   HOH W 145      16.661   4.952  10.161  1.00 41.86      W    O
ATOM   4936  O   HOH W 146      -9.286  -1.522  21.390  1.00 35.03      W    O
ATOM   4939  O   HOH W 147      14.410 -11.209  45.987  1.00 39.95      W    O
ATOM   4942  O   HOH W 148      -1.544 -13.594  23.703  1.00 33.58      W    O
ATOM   4945  O   HOH W 149       4.387   7.952  19.690  1.00 35.86      W    O
ATOM   4948  O   HOH W 150      -8.699  18.279   6.531  1.00 32.48      W    O
ATOM   4951  O   HOH W 151       3.719  -3.684  38.401  1.00 30.50      W    O
ATOM   4954  O   HOH W 152       3.775 -20.312  14.291  1.00 42.65      W    O
ATOM   4957  O   HOH W 153      27.957 -13.614  22.778  1.00 37.15      W    O
ATOM   4960  O   HOH W 154      -6.363  -9.621  22.860  1.00 31.35      W    O
ATOM   4963  O   HOH W 155      17.426  -9.113  39.788  1.00 41.82      W    O
ATOM   4966  O   HOH W 156      11.719  -0.755  38.894  1.00 44.37      W    O
ATOM   4969  O   HOH W 157      -1.823 -18.279  23.964  1.00 31.03      W    O
ATOM   4972  O   HOH W 158       1.236  19.857   5.620  1.00 33.82      W    O
ATOM   4975  O   HOH W 159      -5.447  -2.279   8.958  1.00 43.06      W    O
ATOM   4978  O   HOH W 160       6.495   1.870   6.024  1.00 32.59      W    O
ATOM   4981  O   HOH W 161      -1.902 -10.079  30.428  1.00 40.56      W    O
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ATOM	4984	O	HOH W 162	12.781	-10.832	0.891	1.00	28.70	W	O
ATOM	4987	O	HOH W 163	15.705	-18.496	12.332	1.00	42.03	W	O
ATOM	4990	O	HOH W 164	11.477	23.027	19.258	1.00	43.18	W	O
ATOM	4993	O	HOH W 165	11.794	-19.441	25.110	1.00	34.30	W	O
ATOM	4996	O	HOH W 166	-9.142	6.492	24.586	1.00	37.55	W	O
ATOM	4999	O	HOH W 167	-3.791	-17.095	17.004	1.00	40.54	W	O
ATOM	5002	O	HOH W 168	18.861	-5.381	-3.135	1.00	38.29	W	O
ATOM	5005	O	HOH W 169	1.506	21.043	36.589	1.00	44.96	W	O
ATOM	5008	O	HOH W 170	12.593	-2.711	-7.043	1.00	44.98	W	O
ATOM	5011	O	HOH W 171	15.127	-0.179	0.329	1.00	35.60	W	O
ATOM	5014	O	HOH W 172	15.056	2.474	-0.998	1.00	37.93	W	O
ATOM	5017	O	HOH W 173	-7.283	-6.499	7.178	1.00	49.30	W	O
ATOM	5020	O	HOH W 174	21.316	0.314	-2.427	1.00	41.75	W	O
ATOM	5023	O	HOH W 175	26.651	-5.640	2.963	1.00	36.35	W	O
ATOM	5026	O	HOH W 176	29.087	-10.247	25.287	1.00	39.54	W	O
ATOM	5029	O	HOH W 177	23.713	5.560	13.541	1.00	39.25	W	O
ATOM	5032	O	HOH W 178	-1.768	14.984	-1.759	1.00	40.11	W	O
ATOM	5035	O	HOH W 179	13.927	-22.767	20.107	1.00	44.51	W	O
ATOM	5038	O	HOH W 180	-5.833	17.092	42.432	1.00	39.14	W	O
ATOM	5041	O	HOH W 181	4.780	28.120	30.190	1.00	35.76	W	O
ATOM	5044	O	HOH W 182	5.232	-21.397	10.130	1.00	32.74	W	O
ATOM	5047	O	HOH W 183	-0.609	-13.905	29.169	1.00	42.77	W	O
ATOM	5050	O	HOH W 184	-8.615	-12.423	20.365	1.00	38.88	W	O
ATOM	5053	O	HOH W 185	-2.742	24.869	15.943	1.00	35.44	W	O
ATOM	5056	O	HOH W 186	-6.914	23.870	13.421	1.00	38.92	W	O
ATOM	5059	O	HOH W 187	-9.844	5.148	9.425	1.00	47.06	W	O
ATOM	5062	O	HOH W 188	-3.377	1.908	31.500	1.00	47.62	W	O
ATOM	5065	O	HOH W 189	8.535	-2.717	9.847	1.00	20.99	W	O
ATOM	5068	O	HOH W 190	-2.120	23.920	11.635	1.00	33.73	W	O
ATOM	5071	O	HOH W 191	-1.821	12.406	36.174	1.00	33.31	W	O
ATOM	5074	O	HOH W 192	15.430	-22.456	17.980	1.00	32.67	W	O
ATOM	5077	O	HOH W 193	26.766	-7.447	10.363	1.00	37.80	W	O
ATOM	5080	O	HOH W 194	7.871	-12.672	1.551	1.00	33.24	W	O
ATOM	5083	O	HOH W 195	11.658	-13.419	-1.004	1.00	38.16	W	O
ATOM	5086	O	HOH W 196	16.826	1.526	0.614	1.00	50.30	W	O
ATOM	5089	O	HOH W 197	15.595	6.152	14.916	1.00	40.35	W	O
ATOM	5092	O	HOH W 198	-1.881	25.715	18.176	1.00	37.84	W	O
ATOM	5095	O	HOH W 199	-11.651	11.014	33.297	1.00	32.46	W	O
ATOM	5098	O	HOH W 200	18.893	-2.239	0.202	1.00	36.54	W	O
ATOM	5101	O	HOH W 201	8.083	-15.775	41.296	1.00	35.79	W	O
ATOM	5104	O	HOH W 202	27.247	-8.234	2.554	1.00	45.23	W	O
ATOM	5107	O	HOH W 203	-1.222	-15.328	27.055	1.00	46.27	W	O
ATOM	5110	O	HOH W 204	13.756	-2.002	41.227	1.00	44.19	W	O
ATOM	5113	O	HOH W 205	18.212	11.234	28.397	1.00	46.27	W	O
ATOM	5116	O	HOH W 206	10.446	24.528	22.495	1.00	29.18	W	O
ATOM	5119	O	HOH W 207	9.812	7.702	16.580	1.00	47.51	W	O
ATOM	5122	O	HOH W 208	8.614	13.189	26.746	1.00	42.96	W	O
ATOM	5125	O	HOH W 209	26.242	4.872	13.201	1.00	34.36	W	O
ATOM	5128	O	HOH W 210	3.417	32.021	7.569	1.00	43.78	W	O
ATOM	5131	O	HOH W 211	13.082	12.607	-0.030	1.00	38.29	W	O
ATOM	5134	O	HOH W 212	11.113	-16.047	1.534	1.00	48.53	W	O
ATOM	5137	O	HOH W 213	16.799	-19.980	17.140	1.00	42.01	W	O
ATOM	5140	O	HOH W 214	8.100	2.699	9.516	1.00	38.54	W	O
ATOM	5143	O	HOH W 215	21.192	-10.596	35.721	1.00	42.09	W	O
ATOM	5146	O	HOH W 216	-12.311	27.355	25.513	1.00	46.88	W	O
ATOM	5149	O	HOH W 217	2.196	18.838	8.312	1.00	40.97	W	O
ATOM	5152	O	HOH W 218	2.760	7.802	34.907	1.00	40.65	W	O
ATOM	5155	O	HOH W 219	2.052	34.572	8.653	1.00	28.96	W	O
ATOM	5158	O	HOH W 220	20.199	10.058	26.993	1.00	39.00	W	O
ATOM	5161	O	HOH W 221	0.666	6.917	33.693	1.00	41.05	W	O
ATOM	5164	O	HOH W 222	19.656	-20.516	17.448	1.00	49.29	W	O
ATOM	5167	O	HOH W 223	24.529	-13.997	28.898	1.00	44.80	W	O
ATOM	5170	O	HOH W 224	-15.502	8.924	35.463	1.00	46.22	W	O
ATOM	5173	O	HOH W 225	6.321	6.726	39.047	1.00	40.39	W	O
ATOM	5176	O	HOH W 226	13.346	-19.882	30.564	1.00	27.35	W	O
ATOM	5179	O	HOH W 227	2.475	8.509	20.962	1.00	37.71	W	O
ATOM	5182	O	HOH W 228	25.697	-17.409	7.650	1.00	40.93	W	O

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ATOM   5185  O   HOH W 229      -5.326  22.902  36.076  1.00 34.85      W    O
ATOM   5188  O   HOH W 230      18.689   1.894   1.969  1.00 40.05      W    O
ATOM   5191  O   HOH W 231      22.256   9.449  29.382  1.00 38.70      W    O
ATOM   5194  O   HOH W 232       6.671  16.029  32.045  1.00 45.79      W    O
ATOM   5197  O   HOH W 233     -12.901  11.354  24.852  1.00 42.77      W    O
ATOM   5200  O   HOH W 234      11.146 -21.564   4.017  1.00 44.94      W    O
ATOM   5203  O   HOH W 235      25.034  -1.313  25.290  1.00 35.63      W    O
ATOM   5206  O   HOH W 236     -14.460  18.497  19.730  1.00 43.85      W    O
ATOM   5209  O   HOH W 237     -12.580  11.671  30.829  1.00 49.50      W    O
ATOM   5212  O   HOH W 238     -15.352   9.953  23.232  1.00 41.57      W    O
ATOM   5215  O   HOH W 239      -1.668  11.121  33.395  1.00 56.23      W    O
ATOM   5218  O   HOH W 240       8.754 -13.126  -3.263  1.00 52.79      W    O
ATOM   5221  O   HOH W 241      -1.876  -3.651   6.368  1.00 34.87      W    O
ATOM   5224  O   HOH W 242      19.512 -18.187   6.893  1.00 42.20      W    O
ATOM   5227  O   HOH W 243      -8.077  30.761  18.011  1.00 33.22      W    O
ATOM   5230  O   HOH W 244      11.861  14.174  19.992  1.00 49.09      W    O
ATOM   5233  O   HOH W 245       0.301  11.850  -6.763  1.00 46.36      W    O
ATOM   5236  O   HOH W 246      -2.640  12.555   0.451  1.00 48.51      W    O
ATOM   5239  O   HOH W 247      12.588 -19.822  12.376  1.00 48.93      W    O
ATOM   5242  O   HOH W 248      11.738  20.944  27.362  1.00 51.67      W    O
ATOM   5245  O   HOH W 249      17.071   8.568  19.617  1.00 43.62      W    O
ATOM   5248  O   HOH W 250      -2.350 -17.778  11.732  1.00 51.64      W    O
ATOM   5251  O   HOH W 251      12.306  -4.700  40.223  1.00 48.28      W    O
END
```

Table 3

Alignment of PYK2 with other tyrosine kinase structures

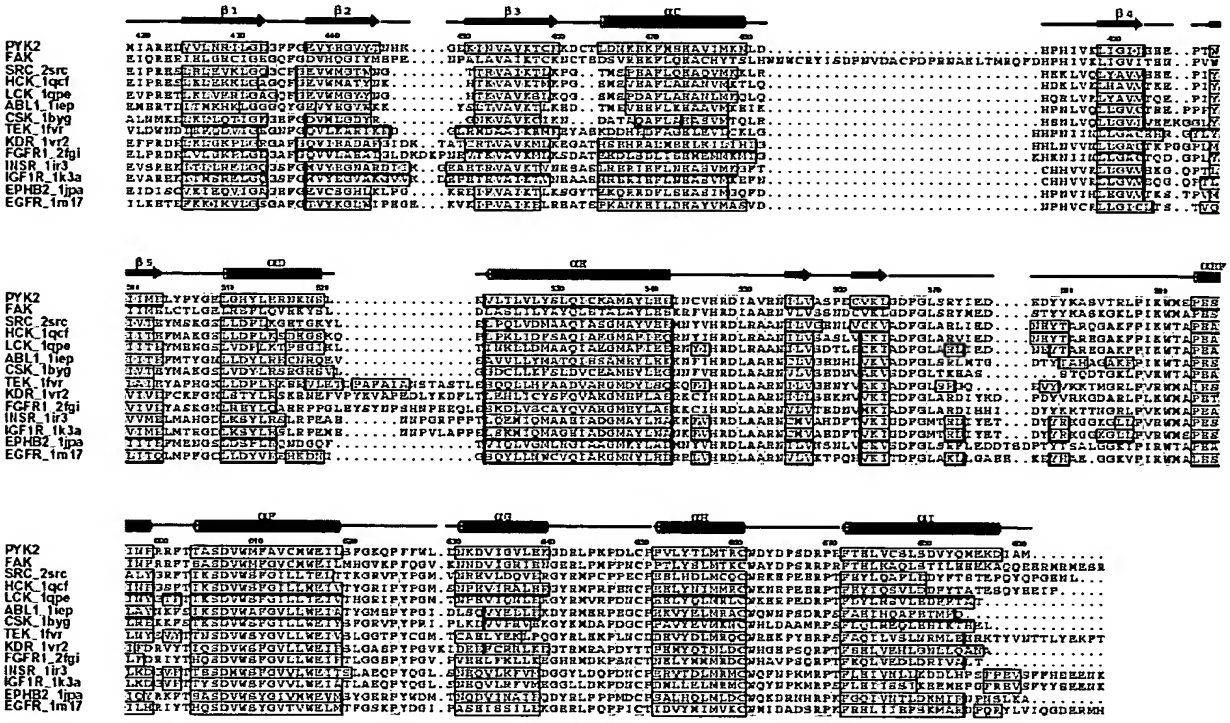

Table 4

PYK2 in pET15S

U33284; Human protein tyrosine kinase PYK2 mRNA, complete cds

Full-length protein in pET15S: 293 aa (SEQ ID NO: 2) Mass: 33872.2 pI: 6.07

PYK2 kinase domain I420-M691 (not including first 21 aa in following sequence) SEQ ID NO: 1

```
  1 MGSSHHHHHH SSGLVPRGSH MIAREDVVLN RILGEGFFGE VYEGVYTNHK GEKINVAVKT
 61 CKKDCTLDNK EKFMSEAVIM KNLDHPHIVK LIGIIEEEPT WIIMELYPYG ELGHYLERNK
121 NSLKVLTLVL YSLQICKAMA YLESINCVHR DIAVRNILVA SPECVKLGDF GLSRYIEDED
181 YYKASVTRLP IKWMSPESIN FRRFTTASDV WMFAVCMWEI LSFGKQPFFW LENKDVIGVL
241 EKGDRLPKPD LCPPVLYTLM TRCWDYDPSD RPRFTELVCS LSDVYQMEKD IAM
```

```
SEQ ID NO: 5
PYK2-C1;        5'-TCCACAG CATATG ATTGCCCGTGAAGATGTGGT-3'      33 mer
SEQ ID NO: 6
PYK2-N2;        TGGAGAAGGACATTGCCATG TAG GTCGAC GAGAG (Origin)
                5'-CTCTC GTCGAC CTA CATGGCAATGTCCTTCTCCA-3'    34 mer
```

pET15S sequence PCR product; 843 bp (SEQ ID NO: 4)
Sequence encoding PYK2 kinase domain (in small letters below) (SEQ ID NO: 3)

```
                                        TCTAGAAATAATTTTGTTTAACTTTAAGAAGGAGA
TATACCATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATG
        attgcc cgtgaagatg
1381 tggtcctgaa tcgtattctt ggggaaggct tttttgggga ggtctatgaa ggtgtctaca
1441 caaatcacaa aggggagaaa atcaatgtag ctgtcaagac ctgcaagaaa gactgcactc
1501 tggacaacaa ggagaagttc atgagcgagg cagtgatcat gaagaacctc gaccacccgc
1561 acatcgtgaa gctgatcggc atcattgaag aggagcccac ctggatcatc atggaattgt
1621 atccctatgg ggagctgggc cactacctgg agcggaacaa gaactccctg aaggtgctca
1681 ccctcgtgct gtactcactg cagatatgca aagccatggc ctacctggag agcatcaact
1741 gcgtgcacag ggacattgct gtccggaaca tcctggtggc ctcccctgag tgtgtgaagc
1801 tgggggactt tggtctttcc cggtacattg aggacgagga ctattacaaa gcctctgtga
1861 ctcgtctccc catcaaatgg atgtccccag agtccattaa cttccgacgc ttcacgacag
1921 ccagtgacgt ctggatgttc gccgtgtgca tgtgggagat cctgagcttt gggaagcagc
1981 ccttcttctg gctggagaac aaggatgtca tcggggtgct ggagaaagga gaccggctgc
2041 ccaagcctga tctctgtcca ccggtccttt ataccctcat gacccgctgc tgggactacg
2101 accccagtga ccggccccgc ttcaccgagc tggtgtgcag cctcagtgac gtttatcaga
2161 tggagaagga cattgccatg
TAGGTCGACTAGAGCCTGCAGTCTCGACCATCATCATCATCATCATTAATAAAAGGGCG
AATTCCAGCACACTGGCGGCCGTTACTAGTGGATCCGGCTGCTAACAAAGCCCGAAAGGAAGCTGAGTTGG
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Table 5: Pyk2 Activity and the Inhibition by ATP Analogs

Pyk2	Vmax	Vmax (SE)	K	K (SE)	K (Lo 95%)	K (Up 95%)	Equation	
8ng/well	1.25e+4	9.11e+2	7.37e+0	2.79e+0	3.27e+0	1.66e+1	y = (Vmax * x) / (K + x)	
Compounds	Vmax	K	K (SE)	K (Lo 95%)	K (Up 95%)	Y2	n	Equation
Adenosine	1.82e+4	2.54e+2	2.65e+2	2.47e+1	2.60e+3	7.33e+2	-5.14e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2
AMP	1.82e+4	8.02e+1	3.76e+1	2.82e+1	2.28e+2	7.33e+2	-5.05e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2
ADT	1.82e+4	1.49e+1	2.69e+0	9.93e+0	2.22e+1	7.33e+2	-7.69e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2
AMPPCP	1.82e+4	7.69e+3	1.99e+4	2.43e+1	2.44e+6	7.33e+2	-2.03e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2
AMPPNP	1.82e+4	1.81e+1	2.82e+0	1.28e+1	2.56e+1	7.33e+2	-7.18e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2
ATP-g-S	1.82e+4	1.36e+1	1.49e+0	1.06e+1	1.73e+1	7.33e+2	-9.66e-1	y = ((Vmax * x^n) / (K^n + x^n)) + Y2